Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information

Formation of steroidal C-25 chiral center *via* asymmetric alkylation methodology

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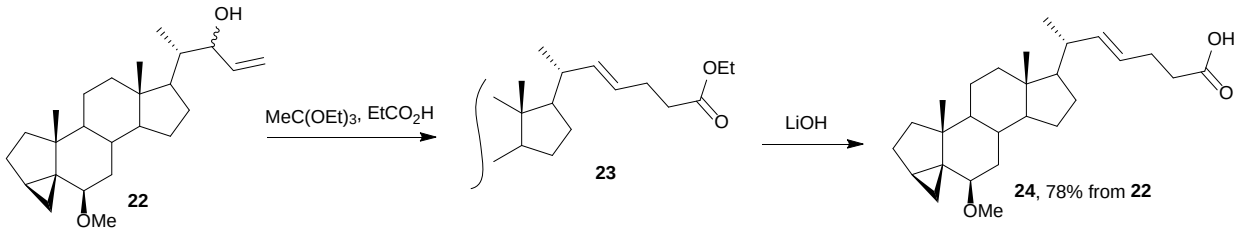
Contents

Experimental section

General remarks

All reactions that required anhydrous conditions were carried out under a positive argon flow with appropriately dried glassware, reagents and solvents. Commercially available reagents were used as received. (-)-(1*S*,2*S*)- and (+)-(1*R*,2*R*)-pseudoephenamines **19** and **20** were synthesized according to the Myers protocol.[1] Commercially available anhydrous LiCl was flame dried under vacuum (0.1 mmHg) for 2−3 min, and iodomethane was filtered through a column of oven-dried basic alumina, both immediately prior to use. The molarity of *n*-butyllithium solutions was determined by titration with menthol against phenanthroline as an indicator (average of three determinations).[2] Petroleum ether (PE) used had a boiling range of 60−90 °C. Reactions were monitored by TLC on silica gel GF_{254} plates. Column chromatography was performed through silica gel (200−300 mesh). One and two-dimensional nuclear magnetic resonance (NMR) spectra were obtained using a Bruker AVANCE 500 spectrometer. Chemical shift values are given in δ (ppm) relative to the residual solvent peaks: δ_H 7.58 and δ_C 135.9 for C_5D_5N; δ_H 7.26 and δ_C 77.0 for $CDCl_3$, and coupling constants are reported in Hz. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), ddd (doublet of doublet of doublets), qd (quartet of doublets), dt (doublet of triplets), sext (sextet). High resolution mass spectra were recorded on a LTQ Orbitrap mass spectrometer coupled to an Accela HPLC System (HPLC column: Hypersyl GOLD, 50 mm × 1 mm, 1.9 μm).

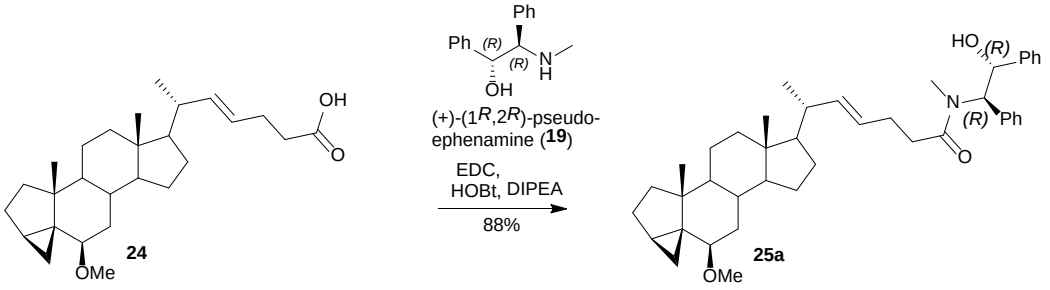
Procedures and spectroscopic analytical data



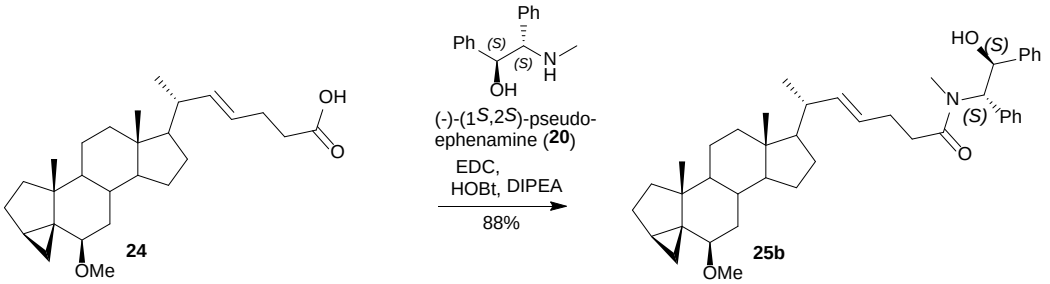
(*E*)-6β-Methoxy-3α,5-cyclo-5α-27-norcholest-22-en-26-oic acid (24). A solution of 6β-methoxy-3α,5-cyclo-5α-chol-23-en-22-ol **22**[3] (2.00 g, 5.37 mmol), triethylorthoacetate (4.92 mL, 26.9 mmol) and propionic acid (401 μL, 5.37 mmol) in toluene (55 mL) was refluxed for 1 h under argon, cooled to ambient temperature, and treated with pyridine (1.3 mL). Evaporation *in vacuo* gave ester **23** (3.4 g) as a crude oil which was directly used in the next step without further purification.

The ester **23** obtained above (3.4 g) was dissolved in THF (40 mL), and then water (13.3 mL) and $LiOH·H_2O$ (0.67 g, 16 mmol) were added to the resulting solution. The mixture was stirred at 65°C for 7 h under argon, and then the solvent was evaporated to half of its initial volume. The residue was diluted with water (10 mL), $CHCl_3$ (20 mL) and acidified with 2N HCl to pH 2. The organic layer was separated, and the water phase was extracted with $CHCl_3$ (3 × 15 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel (PE/EtOAc = 15:1 – 2:1) and recrystallized from hexane to give acid **24** (1.73 g, 78%) as white crystals. Mp: 104-107 °C; $[\alpha]_D^{20}$ = +41.3 (c 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.25 – 5.35 (m, 2H), 3.32 (s, 3H), 2.77 (t, *J* = 2.8 Hz, 1H), 2.36 – 2.42 (m, 2H), 2.25 – 2.30 (m, 2H), 1.98 – 2.07 (m, 1H), 1.94 (dt, *J* = 12.6, 2.8 Hz, 1H), 1.87 (dt, *J* = 6.0, 2.8 Hz, 1H), 1.67 – 1.79 (m, 2H), 1.58 – 1.66 (m, 1H), 1.46 – 1.57 (m, 3H), 1.35 – 1.43 (m, 2H), 1.02 – 1.27 (m, 6H), 1.01 (s, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.76 – 0.90 (m, 4H), 0.71 (s, 3H), 0.64 (t, *J* = 4.5 Hz, 1H), 0.42 (dd, *J* = 7.8, 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.2, 138.6, 124.8, 82.4, 56.5 (2), 55.8, 48.0,

43.3, 42.7, 40.1, 40.0, 35.2, 35.0, 34.2, 33.3, 30.4, 28.5, 27.6, 24.9, 24.1, 22.7, 21.5, 20.5, 19.3, 13.1, 12.4; HRMS (APCI): calcd for $C_{27}H_{43}O_3$ $[M+H]^+$ 415.3207, found 415.3194.

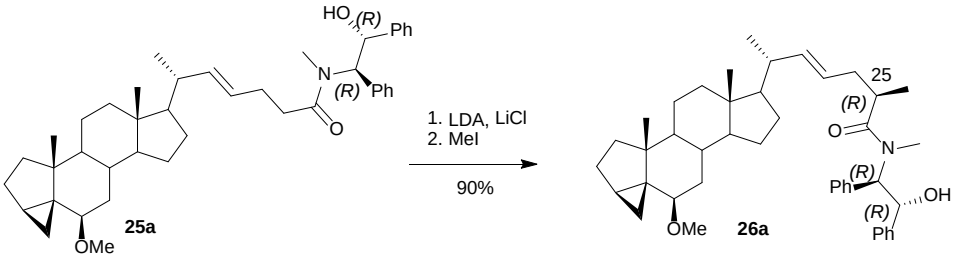


(6*R*,*E*)-*N*-((1*R*,2*R*)-2-Hydroxy-1,2-diphenylethyl)-6-(6β-methoxy-3α,5-cyclo-5α-androstan-17-yl)-*N*-methylhept-4-enamide (25a). *N*,*N*-Diisopropylethylamine (257 µL, 1.48 mmol), 1-hydroxybenzotriazole hydrate (73.1 mg, 0.541 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (104 mg, 0.541 mmol) were added sequentially to a solution of acid **24** (204 mg, 0.492 mmol) and (+)-(1*R*,2*R*)-pseudoephenamine (**19**) (134 mg, 0.590 mmol) in DMF (2 mL). The resulting yellow solution was stirred at room temperature for 18 h, and then partitioned between water (10 mL) and EtOAc (15 mL). The layers were separated, the aqueous layer was extracted with EtOAc (2 × 4 mL). The combined organic extracts were washed sequentially with 1 N HCl (2 × 4 mL), half-saturated aqueous NaCl solution (2 × 4 mL), dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (PE/EtOAc 8:1 – 2:1) to give amide **25a** (271 mg, 88%) as white crystals. Mp: 178-179 °C; $[\alpha]_D^{20}$ = - 51.1 (c 2.2, $CHCl_3$); ^{1}H NMR (6:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.17 – 7.42 (m, 10H), 5.67 (d, *J* = 8.2 Hz, 0.85H), 5.19 – 5.40 (m, 3H), 5.10* (d, *J* = 7.1 Hz, 0.15H), 4.07 (d, *J* = 4.9 Hz, 0.75H), 3.32 (s, 3H), 2.94* (s, 0.45H), 2.86 (s, 2.55H), 2.77 (t, *J* = 2.7 Hz, 1H), 2.15 – 2.42 (m, 4H), 1.92 – 2.06 (m, 2H), 1.85 – 1.91 (m, 1H), 1.68 – 1.81 (m, 2H), 1.59 – 1.68 (m, 1H), 1.47 – 1.59 (m, 3H), 1.35 – 1.45 (m, 2H), 1.00 – 1.27 (m, 9H, containing 1.02 (s, 3H)), 0.98 (d, *J* = 6.6 Hz, 3H), 0.77 – 0.92 (m, 3H), 0.72 (s, 3H), 0.65 (t, *J* = 4.2 Hz, 1H), 0.43 (dd, *J* = 7.8, 5.2 Hz, 1H); ^{13}C NMR (6:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 174.7, 173.7*, 141.8, 141.1*, 137.9, 137.7*, 137.0, 136.9*, 128.6*, 128.5*, 128.4 (4), 128.3 (2), 127.8*, 127.6, 127.5, 127.0*, 126.7 (2), 126.1, 125.8, 82.3, 73.7, 73.4*, 65.4, 56.5 (2), 55.9, 48.0, 43.3, 42.7, 40.1, 39.9, 35.2, 35.0, 34.4, 34.0, 33.5*, 33.3, 30.4, 29.8*, 28.5, 28.2*, 27.9, 24.9, 24.1, 22.7, 21.4, 20.5, 19.2, 13.0, 12.4; HRMS (APCI): calcd for $C_{42}H_{58}NO_3$ $[M+H]^+$ 624.4411, found 624.4404.

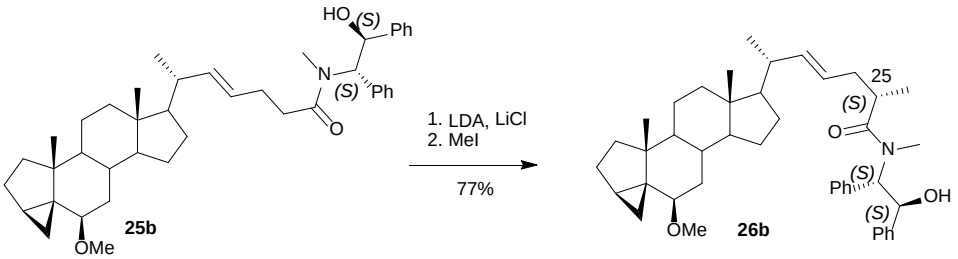


(6*R*,*E*)-*N*-((1*S*,2*S*)-2-Hydroxy-1,2-diphenylethyl)-6-(6β-methoxy-3α,5-cyclo-5α-androstan-17-yl)-*N*-methylhept-4-enamide (25b). The title compound was prepared as white crystals (281 mg, 88%) from acid **24** and (-)-(1*S*,2*S*)-pseudoephenamine (**20**) as described above for the preparation of **25a**. Mp: 158-160 °C; $[\alpha]_D^{20}$ = + 114.7 (c 1.7, $CHCl_3$); ^{1}H NMR (6:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.17 – 7.41 (m, 10H), 5.66 (d, *J* = 8.2 Hz, 0.86H), 5.20 – 5.41 (m, 3H), 5.10* (d, *J* = 7.2 Hz, 0.14H), 4.01 (d, *J* = 3.7 Hz, 0.74H), 3.32 (s, 3H), 2.95* (s, 0.42H), 2.86 (s, 2.58H), 2.77 (t, *J* = 2.6 Hz, 1H), 2.17 – 2.41 (m, 4H), 1.98 – 2.06 (m, 1H), 1.95 (dt, *J* = 12.4, 3.2 Hz, 1H), 1.88 (dt, *J* = 13.5, 2.8 Hz, 1H), 1.70 – 1.80 (m, 2H), 1.59 – 1.68 (m,

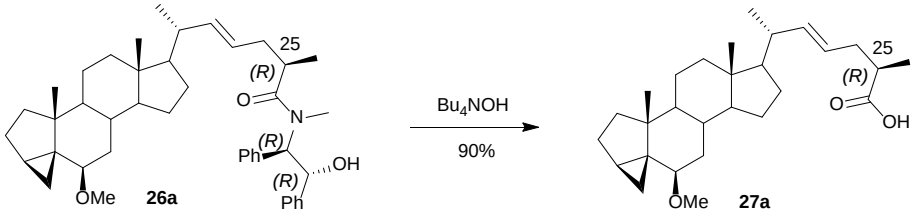
1H), 1.47 – 1.59 (m, 3H), 1.34 – 1.45 (m, 2H), 1.01 – 1.27 (m, 9H, containing 1.02 (s, 3H)), 0.99 (d, *J* = 6.6 Hz, 3H), 0.77 – 0.91 (m, 3H), 0.72 (s, 3H), 0.65 (t, *J* = 4.2 Hz, 1H), 0.43 (dd, *J* = 8.0, 5.1 Hz, 1H); ^{13}C NMR (6:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 174.8, 173.7*, 141.8, 141.0*, 137.9, 137.7*, 137.1, 136.9*, 128.6*, 128.5*, 128.4 (4), 128.3 (2), 127.8*, 127.6, 127.5, 127.0*, 126.7 (2), 126.1*, 125.8, 82.4, 73.8, 73.5*, 65.6, 56.5 (2), 55.9, 48.0, 43.4, 42.7, 40.1, 39.9, 35.2, 35.0, 34.4, 34.1, 33.5*, 33.3, 30.5, 29.8*, 28.6, 28.3*, 27.9, 24.9, 24.1, 22.7, 21.5, 20.5, 19.3, 13.1, 12.4; HRMS (APCI): calcd for $C_{42}H_{58}NO_3$ $[M+H]^+$ 624.4411, found 624.4394.



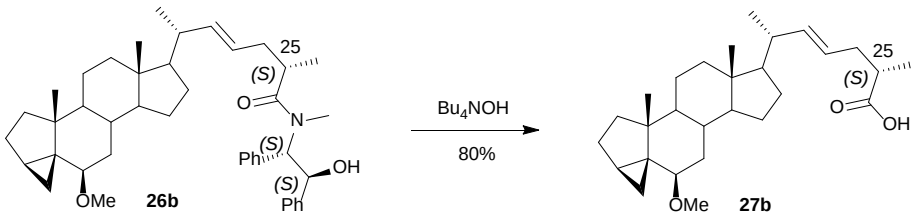
(2*R*,6*R*,*E*)-*N*-((1*R*,2*R*)-2-Hydroxy-1,2-diphenylethyl)-6-(6β-methoxy-3α,5-cyclo-5α-androstan-17-yl)-*N*,2-dimethylhept-4-enamide (26a). *N*,*N*-Diisopropylamine (82 µL, 0.583 mmol) was added to a stirring suspension of lithium chloride (65.6 mg, 1.55 mmol) in THF (0.5 mL) at room temperature. The resulting slurry was cooled to -78 °C and a freshly titrated solution of BuLi in hexane (2.50M, 228µL, 0.570 mmol) was added. The reaction mixture was quickly warmed to 0 °C, stirred for 10 minutes and cooled again to -78 °C. A solution of **25a** (161 mg, 0.258 mmol) in THF (2.1 mL) was added within 10 min. The reaction mixture was stirred for 1 h at -78 ºC, for 15 min at 0 ºC, and for 5 min at 23 ºC, then was cooled to -20 ºC, and then iodomethane (64 µL, 1.03 mmol) was added. After 1.5 h reaction was quenched with saturated aqueous NH_4Cl solution (0.5 mL), warmed to room temperature, diluted with EtOAc (5 mL) and 1:1 mixture of saturated aqueous NaCl solution and 1N HCl (6 mL). The layers were separated; the aqueous layer was extracted with EtOAc (2 × 3 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was chromatographed on silica gel (PE/EtOAc 4:1 – 3:1) to give product **26a** (149 mg, 90%) as pale yellow oil. $[\alpha]_D^{20}$ = - 58.7° (c 0.75, $CHCl_3$); ^{1}H NMR (8:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.18 – 7.43 (m, 10H), 5.46 (d, *J* = 7.4 Hz, 0.9H), 5.38 (t, *J* = 7.0 Hz, 1H), 5.10 – 5.33 (m, 2.1H), 4.55 (br.s, 0.73H), 3.32 (s, 3H), 2.98 (s, 2.6H), 2.86* (s, 0.4H), 2.77 (t, *J* = 2.6 Hz, 1H), 2.55 – 2.67 (m, 1H), 2.27 – 2.35 (m, 1H), 1.91 – 2.07 (m, 3H), 1.87 (dt, *J* = 13.4, 2.8 Hz, 1H), 1.68 – 1.79 (m, 2H), 1.59 – 1.68 (m, 1H), 1.47 – 1.58 (m, 3H), 1.36 – 1.45 (m, 2H), 1.03 – 1.26 (m, 6H), 0.95 – 1.03 (m, 9H), 0.77 – 0.90 (m, 3H), 0.72 (s, 2.6H), 0.68* (s, 0.4H), 0.63 – 0.66 (m, 1H), 0.43 (dd, *J* = 7.9, 5.1 Hz, 1H); ^{13}C NMR (10:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 178.6, 177.7*, 142.0, 139.5, 139.2*, 137.1, 137.0*, 128.6*, 128.5*, 128.4 (2), 128.2 (2), 128.1 (2), 127.7*, 127.5, 127.4, 127.1*, 126.5 (2), 124.6*, 124.5, 82.3, 73.8, 73.4*, 67.2, 65.4*, 56.5 (2), 55.8, 48.0, 43.3, 42.7, 40.1 (2), 37.6*, 37.2, 36.8, 36.4*, 35.2, 35.2, 35.0, 33.3, 30.4, 28.7, 24.9, 24.1, 22.7, 21.4, 20.6, 19.3, 17.4*, 16.9, 13.1, 12.4; HRMS (APCI): calcd for $C_{43}H_{60}NO_3$ $[M+H]^+$ 638.4568, found 638.4561.



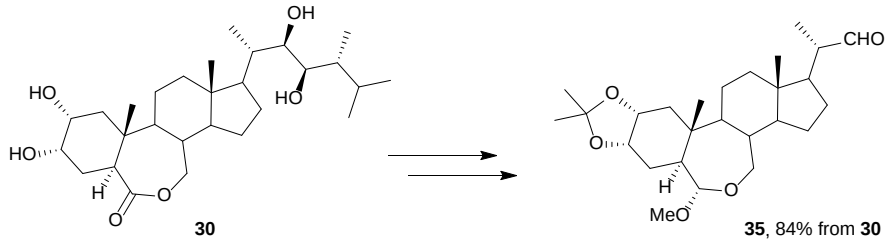
(3*R*,6*R*,*E*)-*N*-((1*S*,2*S*)-2-hydroxy-1,2-diphenylethyl)-6-(6β-methoxy-3α,5-cyclo-5α-androstan-17-yl)-*N*,3-dimethylhept-4-enamide (26b). The title compound was prepared as pale yellow oil (148 mg, 77%) from **25b** as described above for the preparation of **26a**. $[\alpha]_D^{20}$ = + 97.1 (c 1.75, $CHCl_3$); ^{1}H NMR (7:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.18 – 7.42 (m, 10H), 5.50 (d, *J* = 7.5 Hz, 1H), 5.38 (t, *J* = 7.3 Hz, 1H), 5.10 – 5.34 (m, 2H), 4.44 (d, *J* = 5.7 Hz, 1H), 3.32 (s, 3H), 2.98* (s, 3H), 2.86 (s, 3H), 2.76 (t, *J* = 2.8 Hz, 1H), 2.57 – 2.68 (m, 1H), 2.25 – 2.35 (m, 1H), 1.91 – 2.06 (m, 3H), 1.88 (dt, *J* = 13.5, 2.9 Hz, 1H), 1.70 – 1.77 (m, 2H), 1.59 – 1.66 (m, 1H), 1.47 – 1.57 (m, 3H), 1.37 – 1.44 (m, 2H), 1.04 – 1.22 (m, 5H), 0.98 – 1.03 (m, 9H), 0.76 – 0.90 (m, 4H), 0.72 (s, 2.6H), 0.63 – 0.67 (m, 1.4H, containing 0.65* (s, 0.4H)), 0.43 (dd, *J* = 7.9, 5.1 Hz, 1H); ^{13}C NMR (6:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 178.6, 177.6*, 142.0, 139.4, 139.2*, 137.1, 136.9*, 128.6*, 128.5*, 128.4 (2), 128.3 (2), 128.2 (2), 127.8*, 127.5, 127.4, 127.1*, 126.6, 124.5, 124.4, 82.4, 73.9, 73.3*, 66.9, 65.5*, 56.5 (2), 56.0, 48.0, 43.4, 42.7, 42.6*, 40.1, 39.9, 37.7*, 37.2, 36.6, 36.5*, 35.3, 35.1, 35.0, 33.3, 30.4, 28.6, 24.9, 24.1, 22.7, 21.5, 20.5, 19.3, 17.5*, 16.8, 13.0, 12.4; HRMS (APCI): calcd for $C_{43}H_{60}NO_3$ $[M+H]^+$ 638.4568, found 638.4561.



(*E*,25*R*)-6β-Methoxy-3α,5-cyclo-5α-cholest-22-en-26-oic acid (27a). To a stirring biphasic solution of amide **26a** (140 mg, 0.219 mmol) in *t*-BuOH – H_2O (1:1, 2.6 mL), an aqueous solution of tetra-*n*-butylammonium hydroxide (40% w/w, 733μL, 1.10 mmol) was added. The reaction mixture was stirred at 95 °C for 12 h, cooled to room temperature and acidified with 2N HCl to pH 2. The aqueous layer was separated and extracted with EtOAc (2 × 3 mL). The combined organic layers were washed with water (2 × 10 mL), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by column chromatography on SiO_2 (PE/EtOAc 5:1 – 4:1) to give acid **27a** (84.4 mg, 90%, *25R*/*25S* > 99:1 according to ^{13}C NMR spectrum) as colorless oil. $[\alpha]_D^{20}$ = + 27.6 (c 1.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.21 – 5.35 (m, 2H), 3.32 (s, 3H), 2.77 (t, *J* = 2.7 Hz, 1H), 2.48 (sext, *J* = 6.9 Hz, 1H), 2.29 – 2.36 (m, 1H), 2.10 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.00 – 2.06 (m, 1H), 1.91 – 1.97 (m, 1H), 1.85 – 1.90 (m, 1H), 1.69 – 1.80 (m, 2H), 1.59 – 1.67 (m, 1H), 1.47 – 1.58 (m, 3H), 1.36 – 1.43 (m, 2H), 0.95 – 1.24 (m, 16H, containing 1.14 (d, *J* = 6.9 Hz, 3H), 1.01 (s, 3H), 0.98 (d, *J* = 6.6 Hz, 3H)), 0.77 – 0.90 (m, 3H), 0.71 (s, 3H), 0.64 (t, *J* = 4.6 Hz, 1H), 0.42 (dd, *J* = 8.2, 4.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 140.0, 123.5, 82.4, 56.5(2), 55.8, 48.0, 43.4, 42.7, 40.1 (2), 39.6, 36.4, 35.2, 35.0, 33.3, 30.4, 28.6, 24.9, 24.2, 22.7, 21.5, 20.7, 19.3, 16.2, 13.1, 12.4; HRMS (APCI): calcd for $C_{28}H_{45}O_3$ $[M+H]^+$ 429.3363, found 429.3360.



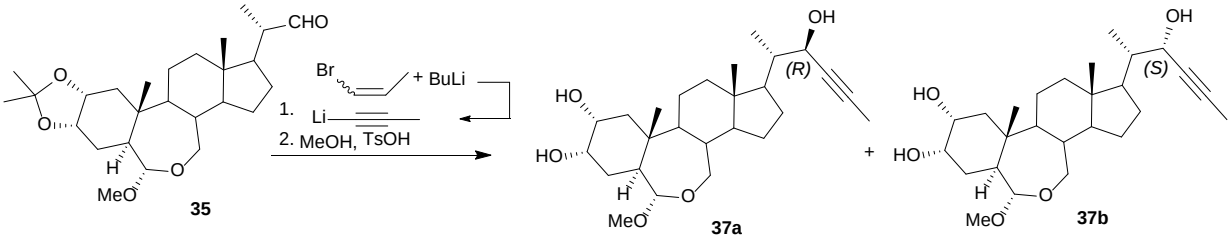
(*E*,25*S*)-6β-Methoxy-3α,5-cyclo-5α-cholest-22-en-26-oic acid (27b). The title compound was prepared as colorless oil (40 mg, 80%, *25S*/*25R* > 99:1 according to ^{13}C NMR spectrum) from amide **26b** as described above for the preparation of **27a**. $[\alpha]_D^{20}$ = + 35.7 (c 1.15, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 – 5.34 (m, 2H), 3.32 (s, 3H), 2.77 (t, *J* = 2.7 Hz, 1H), 2.49 (sext, *J* = 6.9 Hz, 1H), 2.31 (dt, *J* = 13.7, 6.9 Hz, 1H), 2.08 – 2.16 (m, 1H), 1.99 – 2.06 (m, 1H), 1.92 – 1.97 (m, 1H), 1.84 – 1.90 (m, 1H), 1.67 – 1.80 (m, 2H), 1.58 – 1.67 (m, 1H), 1.46 – 1.57 (m, 3H), 1.36 – 1.44 (m, 2H), 0.96 – 1.23 (m, 16H, containing 1.15 (d, *J* = 6.9 Hz, 3H), 1.01 (s, 3H), 0.99 (d, *J* = 6.6 Hz, 3H)), 0.78 – 0.90 (m, 3H), 0.71 (s, 3H), 0.64 (t, *J* = 4.6 Hz, 1H), 0.42 (dd, *J* = 8.0, 4.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.2, 140.0, 123.5, 82.4, 56.6 (2), 55.8, 48.0, 43.4, 42.7, 40.2, 40.1, 39.7, 36.5, 35.2, 35.0, 33.3, 30.4, 28.6, 24.9, 24.2, 22.7, 21.5, 20.7, 19.3, 16.3, 13.1, 12.4. HRMS (APCI): calcd for $C_{28}H_{45}O_3$ $[M+H]^+$ 429.3363, found 429.3360.



(20*S*)-2α,3α-Isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-pregnan-20-carbaldehyde (35). A solution of diisobutylaluminium hydride in toluene (1.1M, 24 mL, 26.4 mmol) was added *via* syringe over 20 min to a stirring solution of 24-epibrassinolide **30** (2.13 g, 4.41 mmol) in THF (40 mL) at -78 °C. The reaction mixture was stirred for additional 40 min, then carefully quenched with MeOH (10 mL), warmed to room temperature, treated with saturated aqueous solution of potassium sodium tartrate (70 mL) and stirred overnight. The layers in the resulting biphasic mixture were separated; aqueous layer was extracted with $CHCl_3$ (3 × 10 mL). The combined organic phases were dried (Na_2SO_4) and evaporated to dryness. The resulting white solid residue (2.43 g) containing lactol **31** was directly used in the next step.

Boric acid (300 mg, 4.85 mmol) was added to a stirring solution of the crude residue obtained above (2.43 g) in THF (50 mL) at room temperature. One hour later the resulting solution of boronic ester was treated with 2,2-dimethoxypropane (9.46 mL, 44.1 mmol) and $TsOH{\cdot}H_2O$ (168 mg, 0.882 mmol). The mixture was stirred for 3 h, then triethylamine (1.84 mL, 13.2 mmol), water (16.7 mL) and $NaIO_4$ (2.83 g, 13.2 mmol) were sequentially added. After stirring for 30 h at room temperature the reaction mixture was diluted with H_2O (80 mL) and EtOAc (30 mL). The organic layer was separated, and the water phase was extracted with EtOAc (2 × 30 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was chromatographed on silica gel (PE/EtOAc 3:1) to afford 1.62 g (84%) of aldehyde **35** as colorless oil. $[\alpha]_D^{20}$ = + 68.0 (c 1.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.54 (d, *J* = 3.2 Hz, 1H), 4.23 – 4.31 (m, 2H), 4.16 (d, *J* = 8.9 Hz, 1H), 3.58 – 3.65 (m, 1H), 3.41 (dd, *J* = 12.7, 2.9 Hz, 1H), 3.29 (s, 3H), 2.33 (dqd, *J* = 10.0, 6.8, 3.2 Hz, 1H), 2.06 – 2.13 (m, 1H), 1.90 – 1.98 (m, 2H), 1.81 – 1.88 (m, 3H), 1.70 – 1.78 (m, 1H), 1.55 – 1.64 (m, 1H), 1.46 – 1.52 (m, 4H, containing 1.48 (s,3H)), 1.34 – 1.46 (m, 2H), 1.18 – 1.35 (m, 9H, containing 1.29 (s,3H)), 1.10 (d, *J* = 6.8 Hz, 3H), 0.97 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.9, 107.7, 104.6, 73.1, 72.9, 64.1, 56.4, 54.7, 51.7, 50.7, 49.5, 43.6, 42.0, 40.6, 40.0,

37.4, 36.4, 28.3, 27.3, 26.9, 24.8, 24.5, 23.3, 17.5, 13.3, 12.5; HRMS (ESI): calcd for $C_{26}H_{46}O_5N$ $[M+NH_4]^+$ 452.3371, found 452.3357.

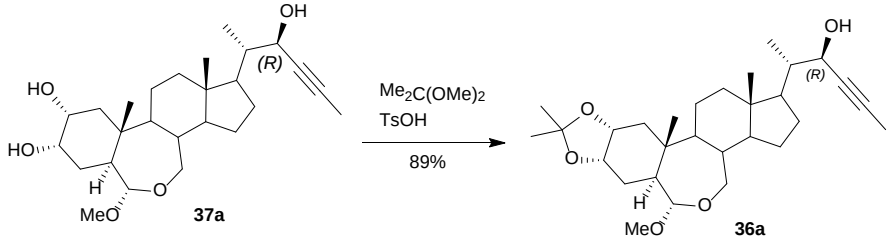


Addition of propynyllithium to aldehyde 35. A solution of BuLi in hexane (2.50M, 1 mL, 2.50 mmol) was added dropwise within 10 min to a stirring solution of (*Z*/*E*)-1-bromopropene (153 µL, 1.78 mmol) in THF (1 mL) at -78 °C. The resulting white suspension was stirred for 2 h at -78 °C and then the solution of aldehyde **35** (500 mg, 1.15 mmol) in THF (2 mL) was slowly added. The reaction mixture was stirred for 1 h, gradually warmed to room temperature (0.5 h) and quenched with saturated aqueous NH_4Cl solution (1 mL). The biphasic mixture was partitioned between EtOAc (3 mL) and water (3 mL), the layers were separated. The aqueous layer was extracted with EtOAc (3 × 3 mL); combined organic phases were dried over Na_2SO_4 and evaporated *in vacuo*.

The resulting residue (580 mg) was dissolved in MeOH (6 mL) and $TsOH \cdot H_2O$ (65.6 mg, 0.345 mmol) was then added. The reaction mixture was kept for 30 min at room temperature, treated with pyridine (0.3 mL) and evaporated to dryness. The crude mixture was chromatographed on silica gel ($CHCl_3$/MeOH 40:1 – 10:1) to give:

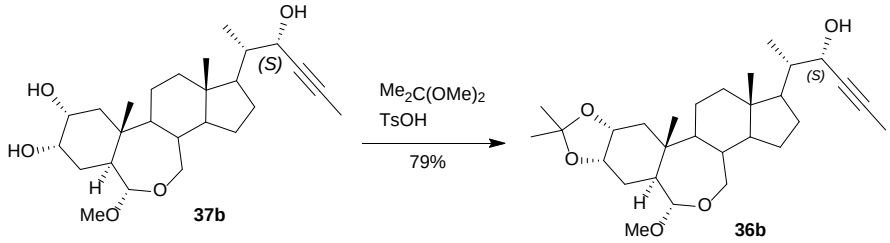
less polar **(22*S*)-2α,3α,22-trihydroxy-6α-methoxy-24-methyl-B-homo-7-oxa-5α-chol-23-yne (37b)** (127 mg, 25%) as white foam. $[\alpha]_D^{20}$ = + 116.7 (c 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.32 – 4.43 (m, 1H), 4.04 (d, *J* = 7.6 Hz, 1H), 3.88 – 4.00 (m, 1H), 3.57 – 3.72 (m, 1H), 3.44 – 3.52 (m, 1H), 3.40 (dd, *J* = 12.2, 1.7 Hz, 1H), 3.28 (s, 3H), 1.62 – 2.12 (m, 13H, containing 2.00 – 2.06 (m, 1H), 1.87 – 1.99 (m, 2H), 1.85 (d, *J* = 1.7 Hz, 3H), 1.75 – 1.82 (m, 2H), 1.63 – 1.74 (m, 3H)), 1.52 – 1.61 (m, 1H), 1.11 – 1.50 (m, 8H), 0.91 – 1.09 (m, 8H, containing 1.01 (d, *J* = 6.5 Hz, 3H) and 0.99 (s, 3H)), 0.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 106.7, 82.1, 77.6, 68.9, 68.1, 65.6, 64.6, 58.6, 54.7, 52.6, 51.4, 42.9, 42.8, 42.1, 42.0, 40.5, 40.1, 39.6, 33.2, 27.6, 24.7, 22.7, 13.5, 12.6, 12.2, 3.7; HRMS (ESI): calcd for $C_{26}H_{46}O_5N$ $[M+NH_4]^+$ 452.3371, found 452.3361.

more polar **(22*R*)-2α,3α,22-trihydroxy-6α-methoxy-24-methyl-B-homo-7-oxa-5α-chol-23-yne (37a)** (337 mg, 67%) as white foam. $[\alpha]_D^{20}$ = + 106.3 (c 1.60, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.37 – 4.45 (m, 1H), 4.03 (d, *J* = 7.7 Hz, 1H), 3.88 – 3.99 (m, 1H), 3.57 – 3.67 (m, 1H), 3.37 – 3.50 (m, 2H), 3.28 (s, 3H), 1.97 – 2.04 (m, 1H), 1.85 – 1.96 (m, 3H), 1.83 (d, *J* = 1.7 Hz, 3H), 1.63 – 1.80 (m, 4H), 1.50 – 1.60 (m, 2H), 1.12 – 1.48 (m, 8H), 1.01 – 1.10 (m, 4H, containing 1.07 (d, *J* = 6.7 Hz, 3H)), 0.98 (s, 3H), 0.88 – 0.95 (m, 1H), 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 106.8, 81.0, 80.4, 69.0, 68.0, 65.3, 64.7, 58.4, 54.7, 51.7, 51.6, 42.8, 42.6, 42.4, 41.9, 40.5, 40.0, 39.6, 33.3, 27.7, 24.6, 22.7, 13.4, 13.0, 11.9, 3.6; HRMS (ESI): calcd for $C_{26}H_{46}O_5N$ $[M+NH_4]^+$ 452.3371, found 452.3363.

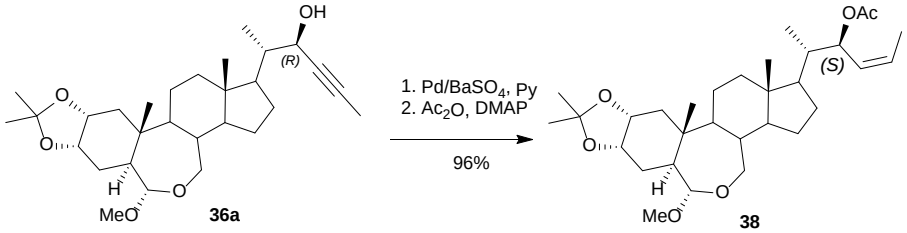


(22*R*)-22-Hydroxy-2α,3α-isopropylidenedioxy-6α-methoxy-24-methyl-B-homo-7-oxa-5α-chol-23-yne (36a). 2,2-Dimethoxypropane (285 µL, 2.30 mmol) and PPTS (19.3 mg, 76.6 µmol) were sequentially added to the solution of triol **37a** (333 mg,

0.766 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was kept for 1 h at room temperature, quenched with Et_3N (107 µL) and evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (PE/EtOAc 6:1 – 2:1) to give 323 mg (89%) of acetonide **36a** as colorless oil. $[\alpha]_D^{20}$ = + 83.8 (c 1.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.37 – 4.43 (m, 1H), 4.22 – 4.31 (m, 2H), 4.15 (d, *J* = 9.0 Hz, 1H), 3.56 – 3.63 (m, 1H), 3.41 (dd, *J* = 12.7, 2.9 Hz, 1H), 3.29 (s, 3H), 2.05 – 2.11 (m, 1H), 1.90 – 1.98 (m, 2H), 1.78 – 1.88 (m, 7H, containing 1.83 (d, *J* = 2.1 Hz, 3H)), 1.67 – 1.75 (m, 1H), 1.64 (d, *J* = 6.2 Hz, 1H, 1.50 – 1.59 (m, 2H), 1.48 (s, 3H), 1.38 – 1.45 (m, 2H), 1.30 – 1.36 (m, 1H), 1.27 – 1.30 (m, 4H, containing 1.28 (s, 3H)), 1.15 – 1.27 (m, 4H), 1.08 (d, *J* = 6.7 Hz, 3H), 0.96 (s, 3H), 0.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 107.7, 104.7, 81.1, 80.4, 73.2, 72.9, 65.5, 64.2, 56.4, 54.7, 52.2, 51.5, 42.9, 42.3, 42.0, 40.7, 40.1, 37.4, 36.4, 28.3, 27.8, 26.9, 24.5, 24.4, 23.4, 17.5, 13.0, 12.1, 3.5; HRMS (ESI): calcd for $C_{29}H_{50}O_5N$ $[M+NH_4]^+$ 492.3684, found 492.3682.



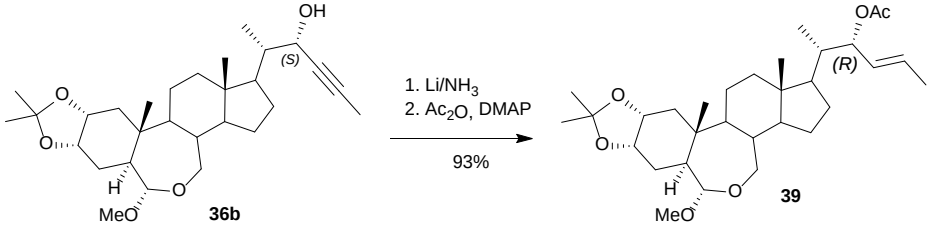
(22*S*)-22-Hydroxy-2α,3α-isopropylidenedioxy-6α-methoxy-24-methyl-B-homo-7-oxa-5α-chol-23-yne (36b). The title compound was prepared as white crystals (301 mg, 79%) from triol **37b** as described above for the preparation of **36a**. Mp: 255-257 °C. $[\alpha]_D^{20}$ = + 35.7 (c 1.15, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.35 – 4.39 (m, 1H), 4.22 – 4.31 (m, 2H), 4.15 (d, *J* = 8.9 Hz, 1H), 3.55 – 3.63 (m, 1H), 3.41 (dd, *J* = 12.6, 2.8 Hz, 1H), 3.29 (s, 3H), 2.04 – 2.11 (m, 1H), 1.89 – 1.99 (m, 3H), 1.77 – 1.88 (m, 6H, containing 1.83 (d, *J* = 2.0 Hz, 3H)), 1.64 – 1.75 (m, 2H), 1.51 – 1.59 (m, 1H), 1.49 (s, 3H), 1.43 (ddd, *J* = 14.6, 11.3, 3.4 Hz, 1H), 1.28 – 1.34 (m, 5H, containing 1.28 (s, 3H)), 1.21 – 1.27 (m, 4H), 1.13 – 1.20 (m, 1H), 1.03 – 1.11 (m, 1H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.96 (s, 3H), 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 107.7, 104.7, 82.0, 77.7, 73.2, 72.9, 65.6, 64.2, 56.4, 54.7, 52.6, 51.9, 43.2, 42.2, 42.1, 40.7, 40.2, 37.5, 36.5, 28.3, 27.6, 27.0, 24.5 (2), 23.4, 17.3, 12.5, 12.4, 3.6; HRMS (ESI): calcd for $C_{29}H_{50}O_5N$ $[M+NH_4]^+$ 492.3684, found 492.3683.



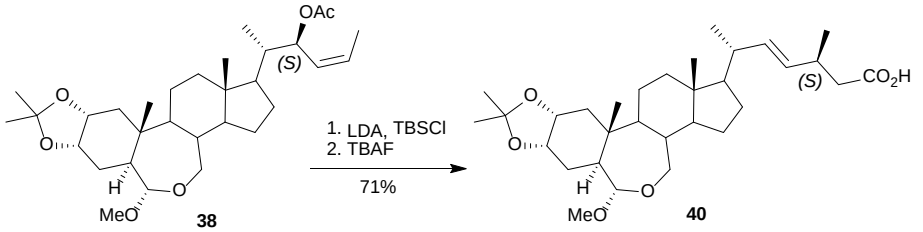
(22*S*,*Z*)-22-Acetoxy-2α,3α-isopropylidenedioxy-6α-methoxy-24-methyl-B-homo-7-oxa-5α-chol-23-ene (38). A mixture of Pd/$BaSO_4$ (131 mg, 5% w/w), propargyl alcohol **36a** (317 mg, 0.668 mmol) and pyridine (3 mL) was vigorously stirred under a hydrogen atmosphere for 5 h, by which time mass-spectrum of an aliquot showed that the reaction was complete. The mixture was filtered through a pad Celite®, the filter cake was washed thoroughly with EtOAc (20 mL). Evaporation gave an oily product (318 mg) which was taken directly to acetylation step.

The product from the previous step (318 mg) was dissolved in CH_2Cl_2 (5 mL). Triethylamine (373 µL, 2.67 mmol), DMAP (12.2 mg, 0.100 mmol) and acetic anhydride (126 µL, 1.34 mmol) were successively added to the resulting solution. The reaction mixture was stirred for 3 h at room temperature and treated with saturated aqueous solution of NH_4Cl (5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL);

combined organic layers were dried over Na_2SO_4 and concentrated to dryness. The residue was chromatographed on silica gel (PE/EtOAc 7:1 – 5:1) to afford 334 mg (96%) of acetate **38** as white crystals. Mp: 140-142 °C; $[\alpha]_D^{20}$ = + 33.3 (c 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.63 (d, *J* = 8.4 Hz, 1H), 5.52 – 5.59 (m, 1H), 5.43 (ddd, *J* = 10.9, 8.4, 1.7 Hz, 1H), 4.22 – 4.31 (m, 2H), 4.16 (d, *J* = 8.9 Hz, 1H), 3.57 – 3.63 (m, 1H), 3.42 (dd, *J* = 12.6, 2.9 Hz, 1H), 3.30 (s, 3H), 2.06 – 2.12 (m, 1H), 2.03 (s, 3H), 1.90 – 1.98 (m, 3H), 1.83 – 1.88 (m, 1H), 1.78 – 1.82 (m, 1H), 1.71 – 1.76 (m, 1H), 1.69 (dd, *J* = 6.7, 1.5 Hz, 3H), 1.51 – 1.59 (m, 2H), 1.50 (s, 3H), 1.40 – 1.46 (m, 1H), 1.33 – 1.39 (m, 1H), 1.28 – 1.32 (m, 4H, containing 1.29 (s, 3H)), 1.14 – 1.28 (m, 5H), 1.03 – 1.11 (m, 1H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.97 (s, 3H), 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 128.8, 126.7, 107.7, 104.7, 73.2, 72.9, 72.6, 64.2, 56.3, 54.7, 52.2 (2), 43.0, 42.0, 41.1, 40.7, 40.2, 37.5, 36.5, 28.3, 28.2, 27.0, 24.5, 24.5, 23.4, 21.3, 17.4, 13.4, 13.3, 12.0; HRMS (ESI): calcd for $C_{31}H_{54}O_6N$ $[M+NH_4]^+$ 536.3946, found 536.3948.

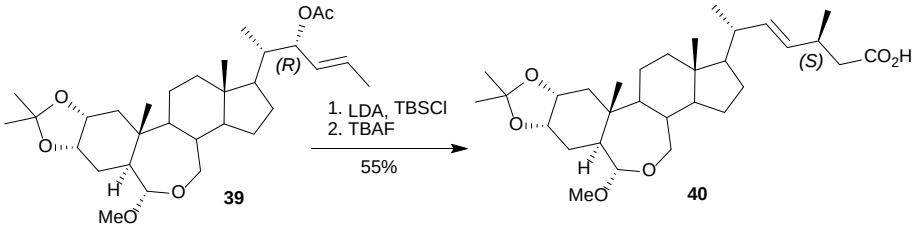


(22*R*,*E*)-22-Acetoxy-2α,3α-isopropylidenedioxy-6α-methoxy-24-methyl-B-homo-7-oxa-5α-chol-23-ene (39). A stirred solution of lithium (29.6 mg, 4.27 mmol) in liquid ammonia (30 mL) at -70 °C was diluted with THF (5 mL), and then the mixture of propargyl alcohol **36b** (289 mg, 0.609 mmol) and *t*-BuOH (408 μL, 4.27 mmol) in THF (15 mL) was added dropwise. The reaction mixture was warmed to -50 °C and stirred at that temperature for 30 min by which time mass-spectrum of an aliquot showed that the reaction was complete. The mixture was treated with solid NH_4Cl (0.2 g), the flask was allowed to warm to room temperature and purged with argon to get rid of ammonia. The resulting mixture was partitioned between $CHCl_3$ (20 mL) and water (20 mL), the aqueous layer was extracted with $CHCl_3$ (2 × 10 mL). The combined organic phases were dried over Na_2SO_4 and evaporated under reduced pressure to give an oily product (288 mg). Its acetylation was carried out in the same manner as for the preparation of **38** to give acetate **39** (293 mg, 93% for two steps) as colorless oil. $[\alpha]_D^{20}$ = + 62.9 (c 1.05, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.72 (dq, *J* = 13.0, 6.4 Hz, 1H), 5.41 (ddd, *J* = 15.3, 8.2, 1.4 Hz, 1H), 5.21 (dd, *J* = 8.2, 3.4 Hz, 1H), 4.21 – 4.31 (m, 2H), 4.15 (d, *J* = 8.9 Hz, 1H), 3.54 – 3.63 (m, 1H), 3.38 – 3.45 (m, 1H), 3.29 (s, 3H), 2.04 – 2.11 (m, 1H), 2.02 (s, 3H), 1.89 – 1.96 (m, 2H), 1.77 – 1.87 (m, 3H), 1.68 – 1.76 (m, 5H, containing 1.71 (dd, *J* = 6.4, 1.1 Hz, 3H)), 1.51 – 1.59 (m, 1H), 1.49 (s, 3H), 1.39 – 1.47 (m, 2H), 1.27 – 1.32 (m, 4H, containing 1.29 (s, 3H)), 1.22 – 1.26 (m, 2H), 1.14 – 1.22 (m, 2H), 0.98 – 1.06 (m, 2H), 0.96 (s, 3H), 0.94 (d, *J* = 6.7 Hz, 3H) 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 130.5, 125.1, 107.6, 104.7, 77.1, 73.2, 72.9, 64.2, 56.3, 54.7, 52.3, 51.9, 43.3, 42.1, 40.6, 40.2, 39.8, 37.4, 36.5, 28.3, 27.6, 27.0, 24.5 (2), 21.5, 18.0, 17.4, 13.0, 12.3; HRMS (ESI): calcd for $C_{31}H_{54}O_6N$ $[M+NH_4]^+$ 536.3946, found 536.3947.

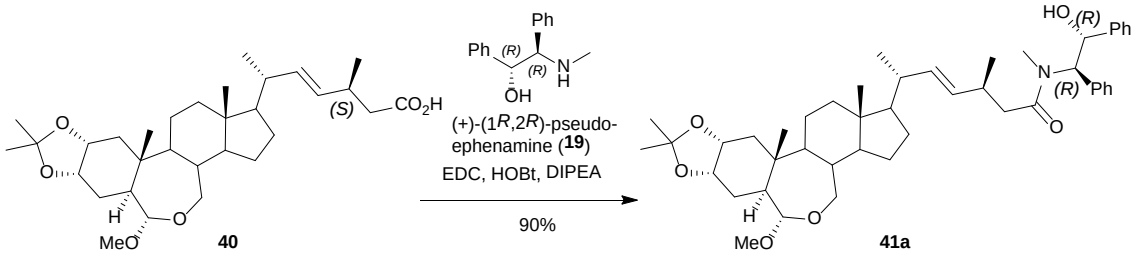


(*E*)-2α,3α-Isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-27-norcampest-22-en-26-oic acid 40. A solution of BuLi in hexane (2.5M, 5.42 mL, 13.6 mmol) was added

to the solution of diisopropylamine (2.00 mL, 14.1 mmol) in THF (6.5 mL) at -78 °C. The reaction mixture was quickly warmed to 0 °C, stirred for 15 minutes and cooled again to -78 °C. The solution of **38** (1.47 g, 2.83 mmol) in THF (7 mL) was added within 10 min. The reaction mixture was stirred for 30 min at -78 °C, and then the solution of TBSCl (3.41 g, 22.6 mmol) in THF – HMPA mixture (7.2 mL, 1:2) was added. After stirring for 15 min at -78 °C, the cooling bath was removed and stirring was continued for 36 h at room temperature. The reaction mixture was treated with TBAF solution in THF (1M, 6 mL, 6 mmol) and stirred for 2 h. Then saturated aqueous solution of NH_4Cl (60 mL), water (60 mL) and EtOAc (40 mL) were added. The organic phase was separated; the aqueous one was extracted with EtOAc (3 × 30 mL). The combined organic layers were successively washed with water (50 mL), saturated aqueous solution of NH_4Cl (50 mL), water (50 mL) and brine (50 mL), dried over Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on SiO_2 (PE/EtOAc 20:1 – 2:1) to give 1.04 g (71%) of acid **40** as pale yellow oil. $[\alpha]_D^{20}$ = + 66.7 (c 1.05, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.17 – 5.30 (m, 2H), 4.23 – 4.31 (m, 2H), 4.16 (d, *J* = 8.9 Hz, 1H), 3.55 – 3.63 (m, 1H), 3.41 (dd, *J* = 12.7, 2.9 Hz, 1H), 3.30 (s, 3H), 2.50 – 2.64 (m, 1H), 2.20 – 2.33 (m, 2H), 2.04 – 2.13 (m, 1H), 1.89 – 2.02 (m, 3H), 1.77 – 1.89 (m, 2H), 1.68-1.76 (m, 1H), 1.55 – 1.64 (m, 1H), 1.40 – 1.51 (m, 5H, containing 1.49 (s, 3H)), 1.08 – 1.33 (m, 11H, containing 1.30 (s, 3H)), 1.02 (d, *J* = 6.7 Hz, 3H), 0.95-0.99 (m, 6H), 0.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.1, 136.1, 131.1, 107.7, 104.8, 73.2, 72.9, 64.2, 56.5, 55.5, 54.7, 52.4, 43.0, 42.1, 41.7, 40.6, 40.2, 39.9, 37.5, 36.5, 33.6, 28.6, 28.3, 27.0, 24.5, 24.4, 23.4, 20.6, 20.5, 17.4, 12.4; HRMS (ESI): calcd for $C_{31}H_{54}O_6N$ $[M+NH_4]^+$ 536.3946, found 536.3947.

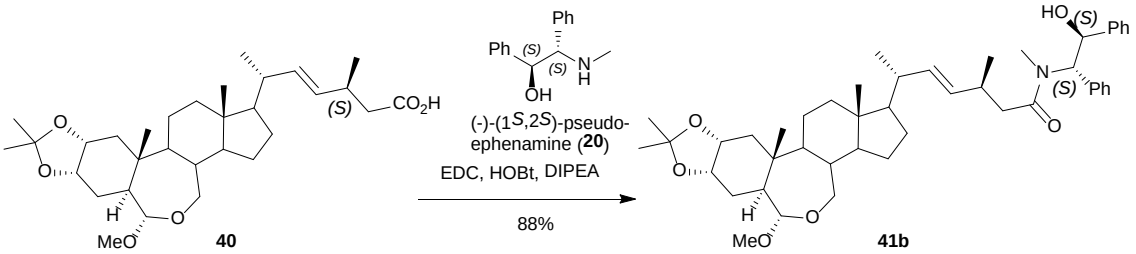


Ireland-Claisen rearrangement of 39 was conducted in the same manner as for **38** to give acid **40** in 55% yield.

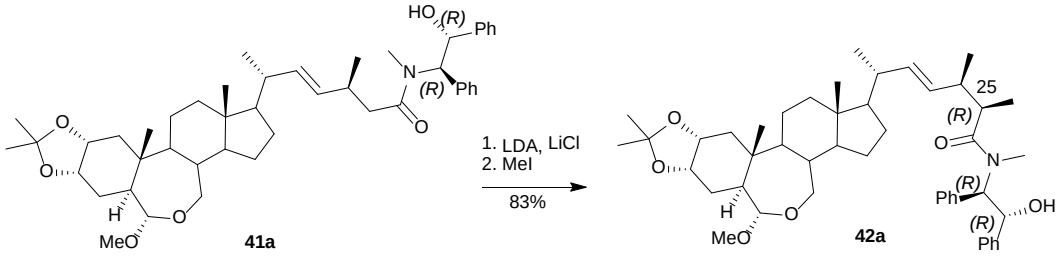


(3*S*,6*R*,*E*)-*N*-((1*R*,2*R*)-2-Hydroxy-1,2-diphenylethyl)-6-(2α,3α-isopropylidenedioxy-6*α*-methoxy-B-homo-7-oxa-5α-androstan-17-yl)-*N*,3-dimethylhept-4-enamide (41a). *N*,*N*-Diisopropylethylamine (615 µL, 3.53 mmol), 1-hydroxybenzotriazole hydrate (175 mg, 1.29 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (248 mg, 1.29 mmol) were added sequentially to a solution of acid **40** (610 mg, 1.18 mmol) and (+)-(1*R*,2*R*)-pseudoephenamine (**19**) (321 mg, 1.41 mmol) in DMF (4.8 ml). The resulting yellow solution was stirred for at room temperature for 18 h, and then partitioned between water (30 mL) and EtOAc (20 mL). The layers were separated; the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic phases were washed with water (2 × 30 mL), brine (30 mL), dried over Na_2SO_4 and evaporated *in vacuo*. The residue was chromatographed on silica gel (PE/EtOAc 3:1 – 2:1) to afford 770 mg (90%) of amide **41a** as pale yellow oil. $[\alpha]_D^{20}$ = - 15.0 (c 1.00, $CHCl_3$). ^{1}H NMR (6:1 rotamer ratio, asterisk denotes minor

rotamer peaks, 500 MHz, $CDCl_3$): δ 7.16 – 7.40 (m, 10H), 5.76 (d, *J* = 8.1 Hz, 0.85H), 5.28 – 5.37 (m, 1H), 5.15 – 5.27 (m, 2H), 5.10* (d, *J* = 7.3 Hz, 0.15H), 4.21 – 4.32 (m, 2H), 4.15 (d, *J* = 8.9 Hz, 1H), 3.92 (d, *J* = 5.1 Hz, 1H), 3.54 – 3.64 (m, 1H), 3.40 (dd, *J* = 12.6, 2.7 Hz, 1H), 3.29 (s, 3H), 2.93* (s, 0.45H), 2.86 (s, 2.55H), 2.58 – 2.68 (m, 1H), 2.30 (dd, *J* = 15.1, 6.5 Hz, 1H), 2.20 (dd, *J* = 15.1, 7.5 Hz, 1H), 2.06 – 2.12 (m, 1H), 1.89 – 1.99 (m, 3H), 1.76 – 1.88 (m, 2H), 1.67 – 1.75 (m, 1H), 1.55 – 1.64 (m, 1H), 1.49 (s, 3H), 1.38 – 1.47 (m, 2H), 1.15 – 1.32 (m, 8H, containing 1.29 (s, 3H)), 1.00 – 1.12 (m, 3H), 0.91 – 0.99 (m, 9H), 0.68 (s, 3H); ^{13}C NMR (9:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 174.1, 141.8, 141.1*, 137.1, 135.2, 132.3*, 132.0, 128.5 (2), 128.3 (2), 128.3 (2), 127.6, 127.4, 127.0*, 126.7 (2), 107.6, 104.7, 73.6, 73.4*, 73.1, 72.9, 65.5*, 64.7, 64.2, 56.4, 55.6, 54.7, 52.4, 42.9, 42.1, 41.3, 40.6, 40.2, 39.8, 37.4, 36.4, 33.8, 33.2*, 33.0, 28.7, 28.3, 27.0, 24.5, 24.4, 23.3, 20.5*, 20.4, 20.3, 17.4, 12.3; HRMS (ESI): calcd for $C_{46}H_{65}O_6NNa$ $[M+Na]^+$ 750.4704, found 750.4704.



(3*S*,6*R*,*E*)-*N*-((1*S*,2*S*)-2-hydroxy-1,2-diphenylethyl)-6-(2α,3α-isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-androstan-17-yl)-*N*,3-dimethylhept-4-enamide (41b). The title compound (676 mg, 88%) was prepared as pale yellow oil from acid **40** and (-)-(1*S*,2*S*)-pseudoephenamine (**20**) as described above for the preparation of **41a**. $[\alpha]_D^{20}$ = + 100.0 (c 1.00, $CHCl_3$); ^{1}H NMR (4:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.14 – 7.40 (m, 10H), 5.62 (d, *J* = 8.0 Hz, 0.73H), 5.33 (t, *J* = 7.2 Hz, 1H), 5.13 – 5.30 (m, 2H), 5.10* (d, *J* = 7.1 Hz, 0.17H), 4.22 – 4.31 (m, 2H), 4.15 (d, *J* = 8.9 Hz, 1H), 4.12 (d, *J* = 5.7 Hz, 0.68H), 3.54 – 3.63 (m, 1H), 3.40 (dd, *J* = 12.6, 2.6 Hz, 1H), 3.29 (s, 3H), 2.92* (s, 0.6H), 2.85 (s, 2.4H), 2.58 – 2.72 (m, 1H), 2.32 (dd, *J* = 15.0, 5.9 Hz, 1H), 2.18 (dd, *J* = 15.0, 8.0 Hz, 1H), 2.04 – 2.13 (m, 1H), 1.92 – 2.02 (m, 3H), 1.76 – 1.88 (m, 2H), 1.68 – 1.75 (m, 2H), 1.57 – 1.66 (m, 1H), 1.49 (s, 3H), 1.39 – 1.47 (m, 2H), 1.18 – 1.32 (m, 8H, containing 1.29 (s, 3H)), 1.01 – 1.14 (m, 3H), 0.91 – 0.99 (m, 9H), 0.68 (s, 2.4H), 0.65* (s, 0.6H); ^{13}C NMR (4:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 174.3, 173.0*, 141.8, 141.2*, 137.1, 135.3*, 135.1, 132.2*, 132.1, 128.5*, 128.4 (2), 128.3 (2), 128.3 (2), 127.6, 127.4, 127.0*, 126.7 (2), 107.6, 104.7, 73.7, 73.5*, 73.1, 72.9, 65.8, 65.4*, 64.2, 56.4, 55.6, 55.5*, 54.7, 52.4, 42.9, 42.1, 41.4, 40.6, 40.2, 39.9*, 39.8, 37.4, 36.4, 34.5, 33.1*, 33.0, 28.7, 28.3, 27.0, 24.5, 24.4, 23.4, 20.6*, 20.4, 20.3, 17.4, 12.3; HRMS (ESI): calcd for $C_{46}H_{65}O_6NNa$ $[M+Na]^+$ 750.4704, found 750.4705.

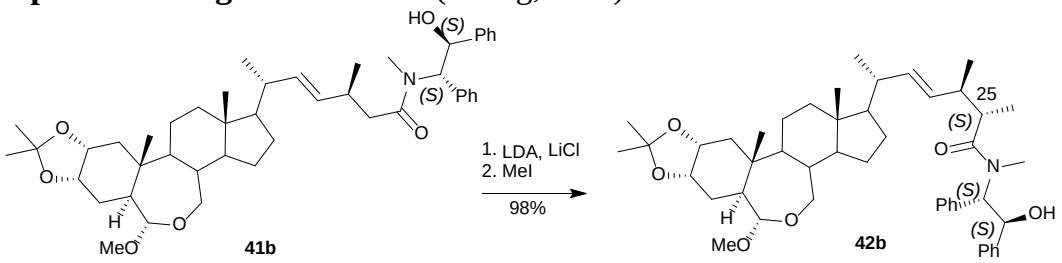


(2*R*,3*R*,6*R*,*E*)-*N*-((1*R*,2*R*)-2-Hydroxy-1,2-diphenylethyl)-6-(2α,3α-isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-androstan-17-yl)-*N*,2,3-trimethylhept-4-enamide (42a). *N*,*N*-Diisopropylamine (167 µL, 1.19 mmol) was added to a stirring suspension of lithium chloride (135 mg, 3.17 mmol) in THF (0.5 mL) at room temperature. The resulting slurry was cooled to -78 °C and a freshly titrated solution of

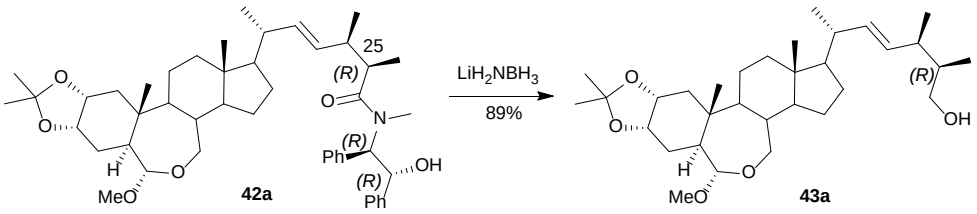
BuLi in hexane (2.45M, 475µL, 1.16 mmol) was added. The reaction mixture was quickly warmed to 0 °C, stirred for 10 minutes and cooled again to -78 °C. A solution of **41a** (385 mg, 0.529 mmol) in THF (2.0 mL) was added within 10 min. The reaction mixture was stirred for 1 h at -78 ºC, for 15 min at 0 ºC, and for 5 min at 23 ºC, cooled to -20 ºC, and then iodomethane (132 µL, 2.12 mmol) was added. After 2 h reaction was quenched with saturated aqueous NH_4Cl solution (1 mL), warmed to room temperature, diluted with EtOAc (7 mL) and water (5 mL). The layers were separated; the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was chromatographed on silica gel (PE/EtOAc 5:1 – 3:1) to give:

less polar compound 42a (325 mg, 83%) as pale yellow oil. $[\alpha]_D^{20}$ = - 31.1 (c 0.45, $CHCl_3$). ^{1}H NMR (11:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.17 – 7.43 (m, 10H), 5.57 (d, *J* = 7.3 Hz, 1H), 5.39 (t, *J* = 6.3 Hz, 1H), 5.25 (dd, *J* = 14.9, 8.8 Hz, 1H), 5.05 (dd, *J* = 14.9, 8.5 Hz, 1H), 4.22 – 4.36 (m, 3H), 4.16 (d, *J* = 8.9 Hz, 1H), 3.60 (t, *J* = 11.7 Hz, 1H), 3.38 – 3.46 (m, 1H), 3.30 (s, 3H), 3.07* (s, 0.25H), 2.87 (s, 2.75H), 2.25 – 2.43 (m, 2H), 2.05 – 2.15 (m, 1H), 1.90 – 2.03 (m, 3H), 1.77 – 1.89 (m, 2H), 1.55 – 1.76 (m, 5H), 1.40 – 1.53 (m, 5H, containing 1.50 (s, 3H)), 1.28 – 1.33 (m, 4H, containing 1.50 (s, 3H)), 1.04 – 1.20 (m, 4H), 0.90 – 1.01 (m, 9H), 0.84 (d, *J* = 6.2 Hz, 3H), 0.69 (s, 3H); ^{13}C NMR (10:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 178.8, 142.0, 137.7, 137.4, 130.9*, 130.6, 128.6*, 128.4 (2), 128.3 (2), 128.3 (2), 127.6, 127.5, 127.2*, 126.8*, 126.6 (2), 107.7, 104.8, 73.8, 73.6*, 73.2, 72.9, 66.5, 66.1*, 64.3, 56.5, 55.7*, 55.6, 54.7, 52.5, 43.0, 42.4, 42.1, 40.7, 40.6, 40.3, 40.2, 37.5, 36.5, 35.2, 29.2, 28.3, 27.0, 24.6 (2), 23.4, 20.6, 20.2*, 20.0, 17.4, 16.6, 12.3; HRMS (ESI): calcd for $C_{47}H_{67}O_6NNa$ $[M+Na]^+$ 764.4861, found 764.4859.

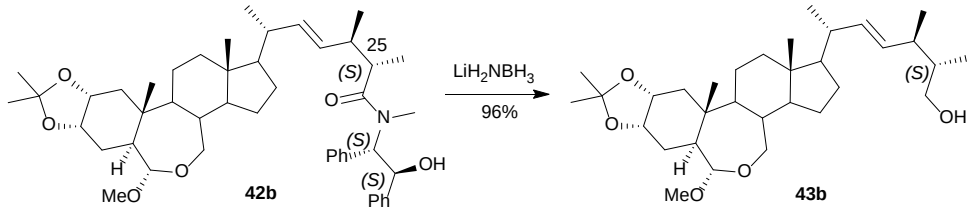
more polar starting material 41a (42 mg, 11%).



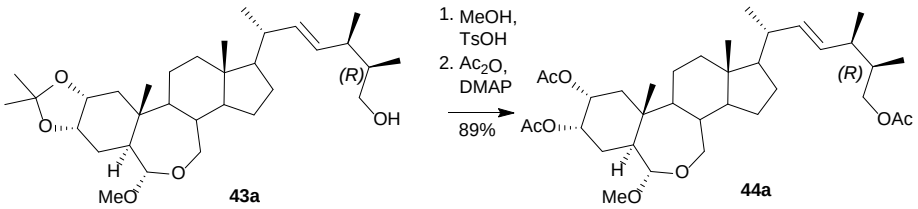
(2*S*,3*R*,6*R*,*E*)-*N*-((1*S*,2*S*)-2-Hydroxy-1,2-diphenylethyl)-6-(2α,3α-isopropylidenedioxy-6*α*-methoxy-B-homo-7-oxa-5α-androstan-17-yl)-*N*,2,3-trimethylhept-4-enamide (42b). The title compound (301 mg, 98%) was prepared as pale yellow oil as described above for the preparation of **42a**. $[\alpha]_D^{20}$ = + 136.8 (c 2.85, $CHCl_3$); ^{1}H NMR (6:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$): δ 7.17 – 7.42 (m, 10H), 5.02 – 5.50 (m, 4H, containing 5.47 (d, *J* = 7.5 Hz, 0.85H)), 4.37 – 4.46 (m, 0.63H), 4.22 – 4.31 (m, 2H), 4.16 (d, *J* = 8.8 Hz, 1H), 3.59 (t, *J* = 11.8 Hz, 1H), 3.41 (dd, *J* = 12.5, 2.4 Hz, 1H), 3.30 (s, 3H), 2.98* (s, 0.45H), 2.86 (s, 2.55H), 2.48 – 2.57 (m, 1H), 2.37 (dd, *J* = 13.4, 6.7 Hz, 1H), 2.05 – 2.13 (m, 1H), 1.89 – 2.03 (m, 3H), 1.82 – 1.88 (m, 1H), 1.56 – 1.82 (m, 4H), 1.49 (s, 3H), 1.40 – 1.47 (m, 2H), 1.27 – 1.34 (m, 5H, containing 1.30 (s, 3H)), 1.01 – 1.22 (m, 5H), 0.94 – 1.00 (m, 9H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.69 (s, 2.55H), 0.55* (s, 0.45H); ^{13}C NMR (10:1 rotamer ratio, asterisk denotes minor rotamer peaks, 125 MHz, $CDCl_3$): δ 178.3, 142.0, 137.3, 136.0, 131.1, 128.6*, 128.5*, 128.4 (4), 128.3 (2), 127.5 (2), 127.1*, 126.6 (2), 107.7, 104.8, 73.9, 73.2, 72.9, 67.1, 64.2, 56.5, 55.8, 55.3*, 54.7, 52.4, 43.0, 42.1, 42.1, 40.6, 40.2, 39.7, 38.0, 37.5, 36.5, 35.3, 28.7, 28.3, 27.0, 24.5, 24.4, 23.4, 20.5*, 20.3, 17.4, 16.0, 14.0, 12.4; HRMS (ESI): calcd for $C_{47}H_{67}O_6NNa$ $[M+Na]^+$ 764.4861, found 764.4857.



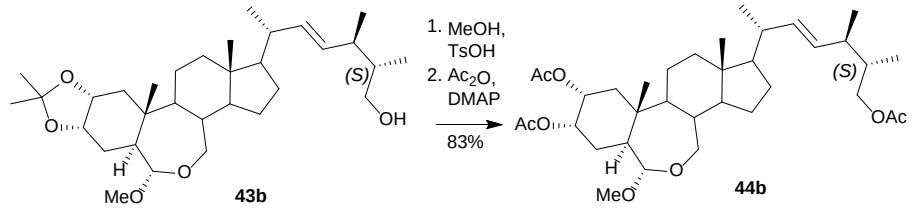
(*E*,25*R*)-26-Hydroxy-2α,3α-isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene (43a). A stirring solution of diisopropylamine (73 µL, 0.521 mmol) in THF (0.5 mL) was cooled to -78 °C and then a solution of BuLi in hexane (2.45M, 202 µL, 0.496 mmol) was added. The resulting solution was warmed to 0 °C and held at this temperature for 15 min. Borane–ammonia complex (90%, 17 mg, 0.551 mmol) was added in one portion, and the suspension was stirred at 0 ºC for 15 min and then was warmed to room temperature. After 15 min the suspension was cooled to 0 ºC, and the solution of amide **42a** (92.1 mg, 0.124 mmol) in THF (0.7 mL) was added. The reaction mixture was warmed to room temperature, stirred for 1.5 h and quenched with saturated aqueous NH_4Cl solution (0.5 mL). After dilution with water (2 mL) and EtOAc (2 mL) the layers were separated. The aqueous layer was extracted with EtOAc (3 × 2 mL), the combined organic phases were were dried over Na_2SO_4 and evaporated under reduced pressure. The crude residue was purified by column chromatography on SiO_2 (PE/EtOAc 5:1 – 4:1) to afford 57.0 mg (89%) of alcohol **43a** as colorless oil. $[\alpha]_D^{20}$ = + 73.4 (c 1.60, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.14 – 5.24 (m, 2H), 4.22 – 4.31 (m, 2H), 4.16 (d, *J* = 8.9 Hz, 1H), 3.59 (dd, *J* = 12.3, 11.2 Hz, 1H), 3.52 (dd, *J* = 10.6, 6.4 Hz, 1H), 3.39 – 3.44 (m, 2H), 3.30 (s, 3H), 2.15 – 2.24 (m, 1H), 2.09 (ddd, *J* = 11.5, 9.0, 3.6 Hz, 1H), 1.91 – 2.02 (m, 3H), 1.83 – 1.88 (m, 1H), 1.78 – 1.82 (m, 1H), 1.68 – 1.76 (m, 1H), 1.53 – 1.68 (m, 2H), 1.49 (s, 3H), 1.39 – 1.47 (m, 2H), 1.29 (s, 3H), 1.16 – 1.27 (m, 5H), 1.01 – 1.16 (m, 3H), 0.94 – 1.00 (m, 9H), 0.83 (d, *J* = 6.9 Hz, 3H), 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.9, 130.2, 107.7, 104.8, 73.2, 72.9, 66.8, 64.2, 56.4, 55.6, 54.7, 52.5, 43.0, 42.1, 40.8, 40.6, 40.3, 40.2, 38.0, 37.5, 36.5, 29.1, 28.3, 27.0, 24.5 (2), 23.4, 20.7, 18.7, 17.4, 12.7, 12.3; HRMS (ESI): calcd for $C_{32}H_{58}O_5N$ $[M+NH_4]^+$ 536.4310, found 536.4310.



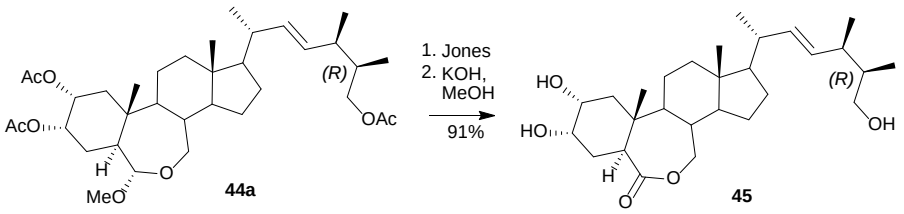
(*E*,25*S*)-26-Hydroxy-2α,3α-isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene (43b). The title compound (179 mg, 96%) was prepared as a colorless oil from amide **42b** as described above for the preparation of **42a**. $[\alpha]_D^{20}$ = + 57.7 (c 0.65, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.12 – 5.30 (m, 2H), 4.22 – 4.31 (m, 2H), 4.15 (d, *J* = 8.9 Hz, 1H), 3.54 – 3.63 (m, 2H), 3.37 – 3.44 (m, 2H), 3.29 (s, 3H), 2.05 – 2.12 (m, 1H), 1.96 – 2.04 (m, 2H), 1.90 – 1.96 (m, 2H), 1.77 – 1.88 (m, 2H), 1.61 – 1.75 (m, 2H), 1.39 – 1.54 (m, 7H, containing 1.49 (s, 3H)), 1.29 (s, 3H), 1.18 – 1.27 (m, 4H), 1.01 – 1.16 (m, 3H), 0.95 – 1.00 (m, 6H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.2, 132.2, 107.7, 104.7, 73.2, 72.9, 66.7, 64.2, 56.4, 55.6, 54.7, 52.5, 43.0, 42.1, 40.9, 40.6, 40.2 (2), 39.1, 37.5, 36.5, 29.0, 28.3, 27.0, 24.5 (2), 23.4, 20.7, 17.6, 17.4, 14.1, 12.3; HRMS (ESI): calcd for $C_{32}H_{58}O_5N$ $[M+NH_4]^+$ 536.4310, found 536.4311.



(*E*,25*R*)-2α,3α,26-Triacetoxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene (44a). *p*-Toluenesulfonic acid monohydrate (13.1 mg, 68.7 μmol) was added to a solution of acetonide **43a** (119 mg, 0.229 mmol) in methanol (2.5 mL). The reaction mixture was held at room temperature for 40 min, treated with Et_3N (96 μL) and concentrated by rotary evaporation. The obtained residue (135 mg) was dissolved in CH_2Cl_2 (1.8 mL). Triethylamine (383 μL, 2.75 mmol), DMAP (4.2 mg, 0.100 mmol) and acetic anhydride (130 μL, 1.37 mmol) were sequentially added to the resulting solution. The reaction mixture was stirred for 1.5 h at room temperature, treated with saturated aqueous solution of NH_4Cl (1.8 mL) and diluted with water (3 mL) and CH_2Cl_2 (3 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 3 mL); combined organic layers were dried over Na_2SO_4 and concentrated to dryness. The residue was chromatographed on silica gel (PE/EtOAc 7:1 – 4:1) to afford 124 mg (89%) of triacetate **44a** as colourless oil. $[\alpha]_D^{20}$ = + 66.7 (c 2.10, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.24 – 5.28 (m, 1H), 5.08 – 5.22 (m, 2H), 4.85 (ddd, *J* = 12.7, 4.4, 2.8 Hz, 1H), 4.03 (d, *J* = 8.0 Hz, 1H), 3.95 (dd, *J* = 10.8, 6.4 Hz, 1H), 3.83 (dd, *J* = 10.8, 7.1 Hz, 1H), 3.38 – 3.50 (m, 2H), 3.27 (s, 3H), 2.11 – 2.18 (m, 1H), 2.09 (s, 3H), 2.02 – 2.07 (m, 4H, containing 2.04 (s, 3H)), 1.96 – 2.01 (m, 4H, containing 1.98 (s, 3H)), 1.93 (dt, *J* = 13.3, 3.2 Hz, 1H), 1.86 (ddd, *J* = 12.4, 8.0, 4.5 Hz, 1H), 1.62 – 1.78 (m, 5H), 1.46 – 1.55 (m, 3H), 1.01 – 1.34 (m, 10H, containing 1.06 (s, 3H)), 0.95 – 0.99 (m, 6H), 0.83 (d, *J* = 6.9 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 170.4 (2), 137.2, 129.7, 106.3, 70.0, 68.1, 67.9, 64.5, 58.7, 55.6, 54.7, 51.9, 43.9, 42.6, 40.4, 40.3, 40.0, 39.6, 39.0, 38.1, 37.6, 30.9, 29.0, 24.6, 22.8, 21.2, 21.1, 21.0, 20.7, 18.6, 13.5, 12.9, 12.2; HRMS (ESI): calcd for $C_{35}H_{56}O_8Na$ $[M+Na]^+$ 627.3867, found 627.3871.

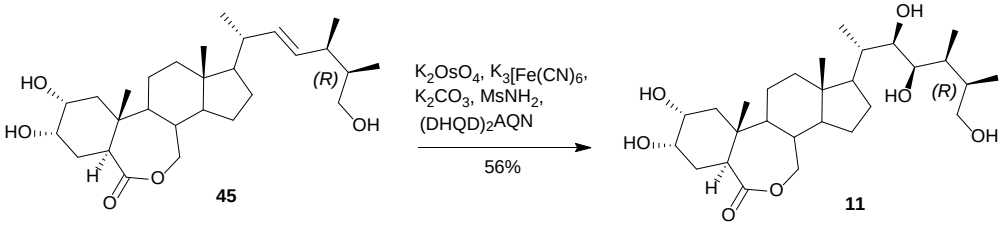


(*E*,25*S*)-2α,3α,26-Triacetoxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene (44b). The title compound (100 mg, 83%) was prepared as colorless oil from acetonide **43b** as described above for the preparation of **44a**. $[\alpha]_D^{20}$ = + 57.2 (c 1.53, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.24 – 5.28 (m, 1H), 5.12 – 5.23 (m, 2H), 4.85 (ddd, *J* = 12.7, 4.5, 2.8 Hz, 1H), 4.00 – 4.09 (m, 2H), 3.79 (dd, *J* = 10.8, 7.7 Hz, 1H), 3.38 – 3.51 (m, 2H), 3.27 (s, 3H), 2.09 (s, 3H), 2.01 – 2.06 (m, 5H, containing 2.03 (s, 3H)), 1.96 – 2.01 (m, 4H, containing 1.98 (s, 3H)), 1.93 (dt, *J* = 12.3, 2.9 Hz, 1H), 1.86 (ddd, *J* = 12.4, 8.0, 4.5 Hz, 1H), 1.61 – 1.78 (m, 5H), 1.46 – 1.55 (m, 3H), 1.00 – 1.35 (m, 10H, containing 1.06 (s, 3H)), 0.97 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 170.4 (2), 136.5, 131.3, 106.3, 70.0, 68.0 (2), 64.5, 58.8, 55.7, 54.7, 52.0, 43.9, 42.6, 40.4, 40.2, 40.0, 39.6, 39.0, 38.8, 37.5, 30.9, 28.9, 24.6, 22.8, 21.2, 21.1, 21.0, 20.6, 17.1, 14.1, 13.5, 12.2; HRMS (ESI): calcd for $C_{35}H_{56}O_8Na$ $[M+Na]^+$ 627.3867, found 627.3872.



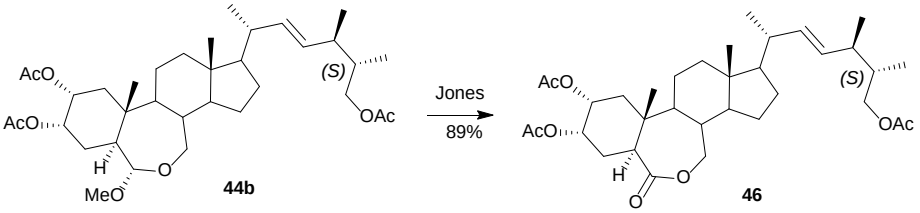
(*E*,25*R*)-2α,3α,26-Trihydroxy-B-homo-7-oxa-5α-campest-22-en-6-one (45). Jones reagent (0.5 mL; prepared from 2.67 g CrO_3, 2.3 mL H_2SO_4, then diluted to 10 mL with water) was added dropwise to the stirring solution of **44a** (120 mg, 0.198 mmol) in acetone (3.5 mL) at 0 °C. After 50 min a new portion of oxidant (0.3 mL) was added. The reaction mixture was stirred for additional 20 min (0 °C) by which time TLC indicated that the oxidation was completed. The excess of Jones reagent was destroyed by addition of *i*-PrOH (2 mL) and stirring the obtained mixture at 0 °C for 10 min. The obtained heterogeneous mixture was diluted with water (10 mL) and $CHCl_3$ (5 mL). The layers were separated; the aqueous layer was extracted with $CHCl_3$ (2 × 3 mL). The combined organic phases were washed with saturated solution of $NaHCO_3$ (5 mL), dried over Na_2SO_4 and evaporated *in vacuo* to give crude triacetoxylactone (125 mg), which was directly used in the next step.

The crude residue obtained above (125 mg) was treated with the solution of KOH in methanol (5% w/w, 5 mL) at room temperature for 15 min. The reaction mixture was acidified with 2N HCl to pH 3 and diluted with water (10 mL) and $CHCl_3$ (10 mL). The organic layer was separated; the aqueous one was extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The resulting residue was purified by column chromatography on SiO_2 ($CHCl_3$/MeOH 20:1 – 15:1) to afford 84.0 mg (91%) of triol **45** as white crystals. Mp: 284-286 °C. $[\alpha]_D^{20}$ = + 44.9 (c 1.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.10 – 5.30 (m, 2H), 3.98 – 4.13 (m, 3H), 3.66 – 3.77 (m, 1H), 3.53 (dd, *J* = 10.6, 6.5 Hz, 1H), 3.43 (dd, *J* = 10.6, 6.3 Hz, 1H), 3.11 (dd, *J* = 12.0, 3.6 Hz, 1H), 2.09 – 2.40 (m, 3H), 1.91 – 2.09 (m, 4H), 1.87 (dd, *J* = 12.3, 3.9 Hz, 1H), 1.65 – 1.80 (m, 3H), 1.52 – 1.64 (m, 3H), 1.40 (qd, *J* = 13.5, 3.3 Hz, 1H), 1.05 – 1.32 (m, 7H), 0.94 – 1.02 (m, 6H), 0.91 (s, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.6, 136.5, 130.6, 70.5, 68.0 (2), 66.7, 58.1, 55.6, 51.4, 42.4, 41.3, 40.9, 40.7, 40.2, 39.4, 39.0, 38.3, 37.9, 31.1, 28.5, 24.8, 22.1, 20.7, 18.6, 15.4, 12.7, 11.9; HRMS (ESI): calcd for $C_{28}H_{47}O_5$ $[M+H]^+$ 463.3418, found 463.3417.

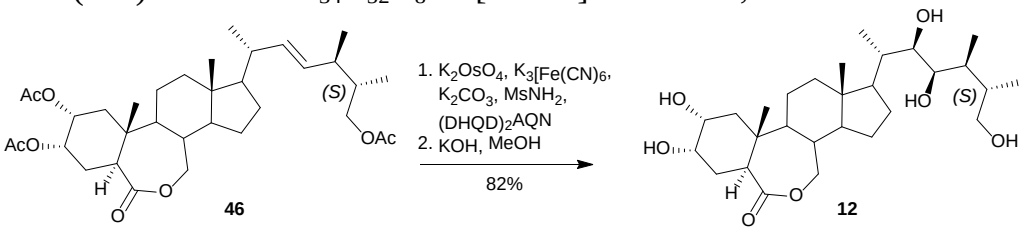


(22*R*,23*R*,25*R*)-2α,3α,22,23,26-Pentahydroxy-B-homo-7-oxa-5α-campestan-6-one (11). Water (1.4 mL), $K_3[Fe(CN)_6]$ (107 mg, 0.325 mmol), K_2CO_3 (44.9 mg, 0.325 mmol), methanesulfonamide (15.4 mg, 0.162 mmol), $(DHQD)_2AQN$ (4.6 mg, 5.4 μmol), $K_2OsO_4 \cdot 2H_2O$ (0.8 mg, 2.16 μmol) were sequentially added to the solution of olefin **45** (50 mg, 0.11 mmol) in t-BuOH (1.4 mL). The reaction mixture was stirred for 20 h at room temperature, whereupon Na_2SO_3 (163 mg, 1.30 mmol) was added and stirring was continued for additional 2 h. The reaction mixture was diluted with water (5 mL) and chloroform (5 mL), and then brine (5 mL) was added to the resulting clear biphasic solution. The organic layer was separated, the aqueous phase was extracted with $CHCl_3$-MeOH mixture (3:1, 4 × 5 mL). The combined organic phases were dried over Na_2SO_4 and evaporated under reduced pressure. The resulting residue was

chromatographed on silica gel (EtOAc/AcOH 2:1). The fractions, containing steroid were evaporated and purified by column chromatography on SiO_2 ($CHCl_3$/MeOH 20:1 – 9:1) to give 30.0 mg (56%) of pentaol **11** as white crystals. Mp: 284-286 °C; lit.[4] 305-306 °C $[\alpha]_D^{20}$ = + 36.8 (c 0.38, $CHCl_3$:MeOH – 1:1); ^{1}H NMR (500 MHz, C_5D_5N) δ 4.40 – 4.49 (m, 1H), 4.16 – 4.24 (m, 1H), 3.96 – 4.12 (m, 5H), 3.82 – 3.90 (m, 1H), 3.61 (dd, *J* = 12.1, 4.0 Hz, 1H), 2.48 – 2.56 (m, 1H), 2.28 – 2.38 (m, 1H), 2.04 – 2.28 (m, 5H), 1.98 – 2.05 (m, 1H), 1.89 – 1.97 (m, 2H), 1.66 – 1.83 (m, 3H), 1.51 (s, 1H), 1.36 – 1.46 (m, 1H), 1.18 – 1.33 (m, 13H), 1.06 – 1.18 (m, 3H), 0.98 – 1.06 (m, 4H, containing 1.04 (s,3H)), 0.67 (s, 3H); ^{13}C NMR (125 MHz, C_5D_5N) δ 177.1, 74.6, 74.5, 70.6, 69.1, 68.8, 65.1, 58.7, 53.3, 51.9, 43.1, 42.9, 42.1, 40.8, 40.4, 40.1, 38.9, 38.6, 37.9, 33.5, 28.5, 25.3, 22.9, 17.2, 16.3, 13.1, 12.2, 10.0; HRMS (ESI): calcd for $C_{28}H_{49}O_7$ $[M+H]^+$ 497.3473, found 497.3473.



(*E*,25*S*)-2α,3α,26-Triacetoxy-B-homo-7-oxa-5α-campest-22-en-6-one (46). Oxidation of lactol methyl acetal **44b** to lactone **46** was conducted in the same manner as described for **44a**. The crude residue after extraction and evaporation was chromatographed on silica gel (PE/EtOAc 4:1 – 2:1) to afford (62 mg, 89%) of lactone **46** as white crystals. Mp: 189-190 °C. $[\alpha]_D^{20}$ = + 48.5 (c 0.65, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.31 – 5.39 (m, 1H), 5.12 – 5.23 (m, 2H), 4.85 (ddd, *J* = 12.7, 4.0, 2.8 Hz, 1H), 3.99 – 4.15 (m, 3H), 3.79 (dd, *J* = 10.7, 7.8 Hz, 1H), 2.99 (dd, *J* = 12.3, 4.2 Hz, 1H), 2.22 – 2.33 (m, 1H), 2.10 (s, 3H), 2.01 – 2.05 (m, 4H, containing 2.03 (s, 3H)), 1.94 – 2.00 (m, 4H, containing 1.98 (s, 3H)), 1.87 – 1.94 (m, 2H), 1.58 – 1.77 (m, 6H), 1.40 (ddd, *J* = 16.2, 13.4, 3.6 Hz, 1H), 1.10 – 1.33 (m, 7H), 0.96 – 1.00 (m, 6H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.1, 171.2, 170.2, 170.0, 136.1, 131.6, 70.5, 68.9, 67.9 (2), 58.3, 55.7, 51.4, 42.4, 42.0, 40.1, 39.3, 39.0, 38.8 (2), 38.4, 37.5, 29.3, 28.4, 24.8, 22.2, 21.1, 21.0 (2), 20.7, 17.1, 15.4, 14.1, 11.9; HRMS (ESI): calcd for $C_{34}H_{52}O_8Na$ $[M+Na]^+$ 611.3554, found 611.3552.



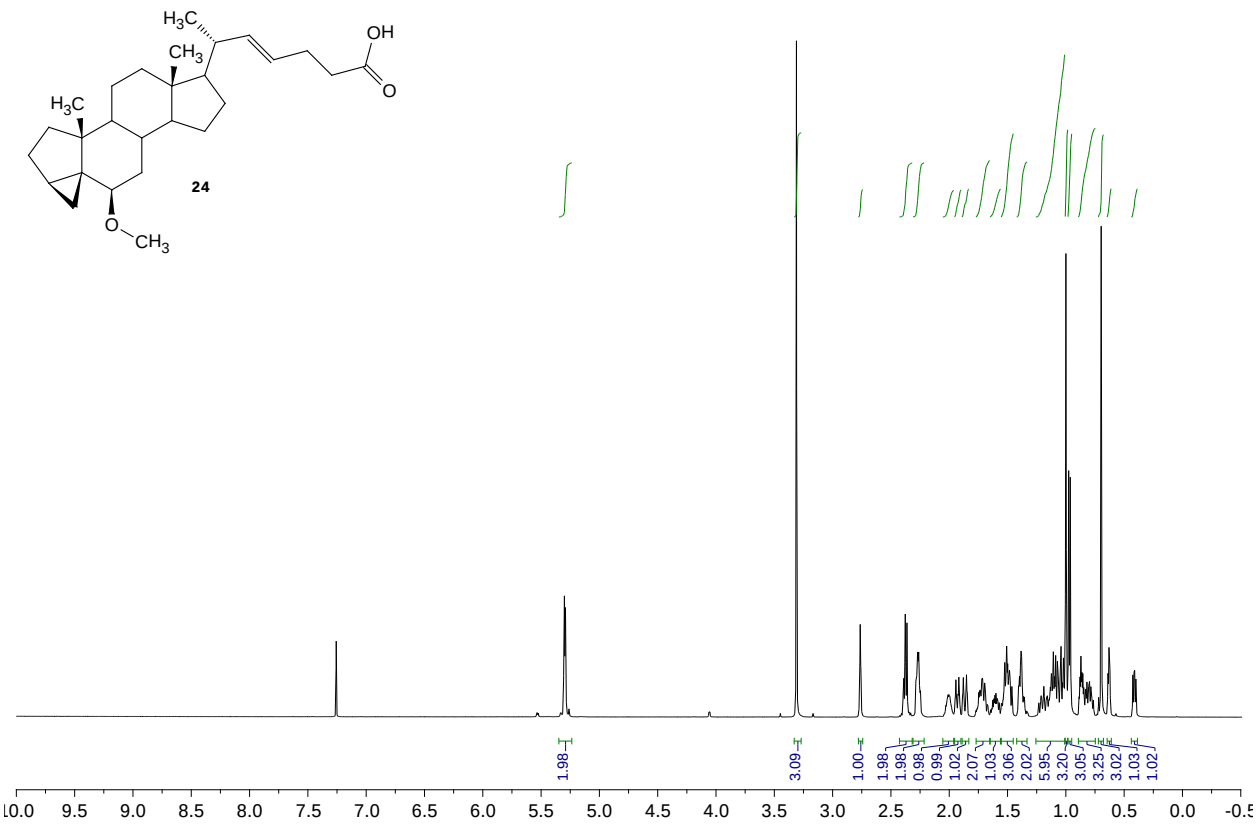
(22*R*,23*R*,25*S*)-2α,3α,22,23,26-Pentahydroxy-B-homo-7-oxa-5α-campestan-6-one (12). Water (1.4 mL), $K_3[Fe(CN)_6]$ (82.3 mg, 0.250 mmol), K_2CO_3 (34.6 mg, 0.250 mmol), methanesulfonamide (11.9 mg, 0.125 mmol), $(DHQD)_2AQN$ (3.6 mg, 4.17 μmol), $K_2OsO_4 \cdot 2H_2O$ (0.6 mg, 1.67 μmol) were sequentially added to the solution of olefin **46** (50 mg, 0.11 mmol) in t-BuOH (2 mL). The reaction mixture was stirred for 5 h at room temperature, whereupon Na_2SO_3 (126 mg, 1.00 mmol) was added and stirring was continued for additional 40 min. The reaction mixture was partitioned between water (5 mL) and chloroform (10 mL). The aqueous layer was extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and evaporated *in vacuo*. The resulting residue was chromatographed on silica gel (EtOAc). The fractions, containing steroids were evaporated to give crude mixture (57.1 mg), free of $(DHQD)_2AQN$.

The mixture obtained above (57.1 mg) was treated with a solution of KOH in methanol (5% w/w, 5 mL) at room temperature for 15 min. The reaction mixture was acidified with

2N HCl to pH 3 and diluted with water (5 mL) and chloroform (5 mL). Brine (5 mL) was added to the resulting clear biphasic solution. The layers were separated, the aqueous layer was extracted with $CHCl_3$-MeOH mixture (3:1, 4 × 4 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by column chromatography on SiO_2 ($CHCl_3$/MeOH 20:1 – 9:1) to afford 34.1 mg (82%) of pentaol **12** as white crystals. Mp: 293-296 °C; $[\alpha]_D^{20}$ = + 45.8 (c 0.77, $CHCl_3$:MeOH – 1:1); ^{1}H NMR (500 MHz, C_5D_5N) δ 4.40 – 4.48 (m, 1H), 4.23 – 4.30 (m, 1H), 3.98 – 4.11 (m, 5H), 3.92 – 3.97 (m, 1H), 3.61 (dd, *J* = 12.0, 4.1 Hz, 1H), 2.47 – 2.56 (m, 1H), 2.28 – 2.37 (m, 1H), 2.02 – 2.24 (m, 6H), 1.88 – 1.99 (m, 2H), 1.66 – 1.83 (m, 3H), 1.47 – 1.57 (m, 1H), 1.36 – 1.46 (m, 1H), 1.19 – 1.34 (m, 13H), 1.06 – 1.17 (m, 3H), 0.99 – 1.06 (m, 4H, containing 1.04 (s, 3H)), 0.69 (s, 3H); ^{13}C NMR (125 MHz, C_5D_5N) δ 177.1, 74.5, 73.6, 70.7, 69.1, 68.8, 65.1, 58.7, 53.3, 51.9, 43.1, 43.0, 42.1, 40.6, 40.5, 40.1, 38.9, 38.7, 37.1, 33.5, 28.5, 25.3, 22.9, 16.3, 16.2, 13.1, 12.2, 11.4; HRMS (ESI): calcd for $C_{28}H_{49}O_7$ $[M+H]^+$ 497.3473, found 497.3473.

References

1. M. R. Morales, K. T. Mellem and A. G. Myers, *Angew. Chem. Int. Ed. Engl.*, 2012, **51**, 4568-4571.
2. H.-S. Lin and L. A. Paquette, *Synth. Commun.*, 1994, **24**, 2503-2506.
3. R. D. Walkup, G. D. Anderson and C. Djerassi, *Tetrahedron Lett.*, 1979, **20**, 767-770.
4. T. G. Back, S. K. Nakajima and J. L. Zhu, *Synlett*, 2000, 1649-1651.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2.07
1.03
3.06
2.02
5.95
3.20
3.05
3.25
3.02
1.03
1.02
10.0
9.5
9.0
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8.0
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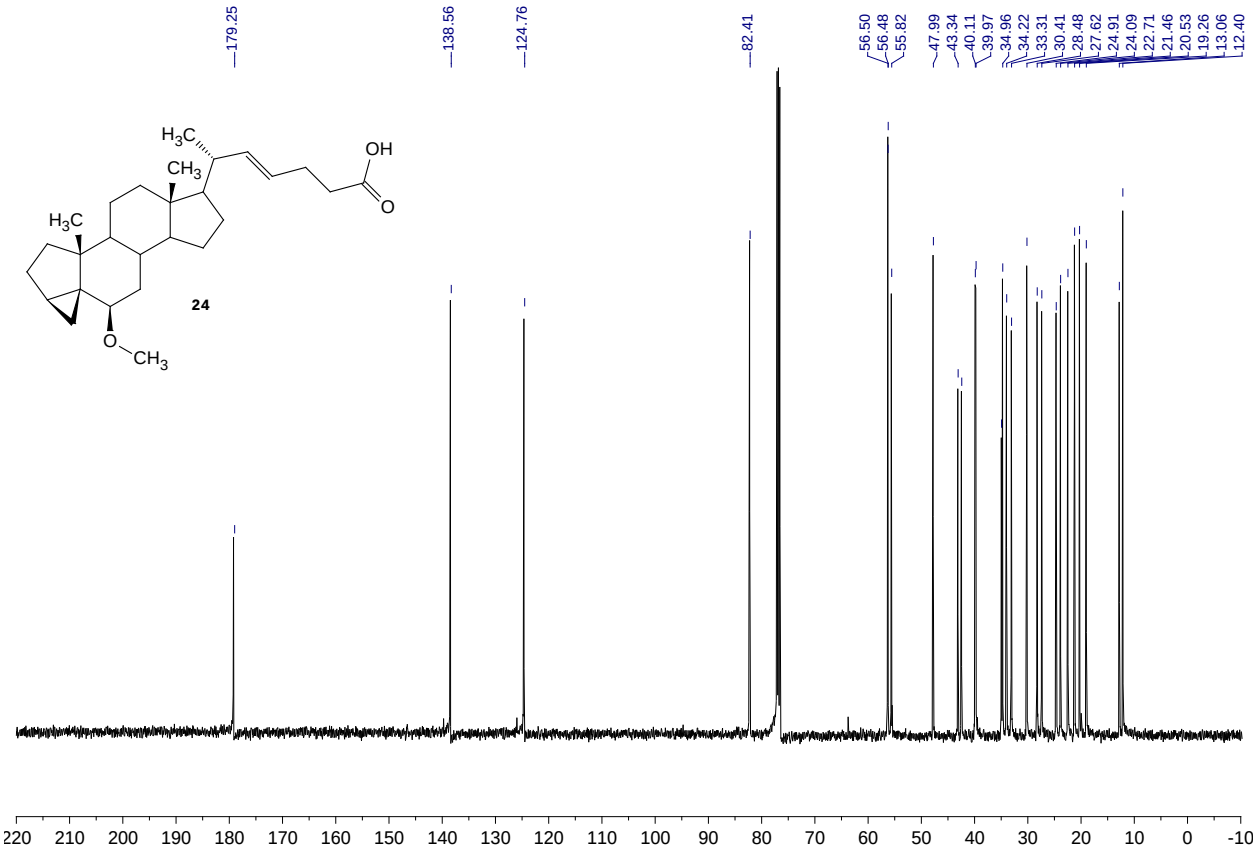
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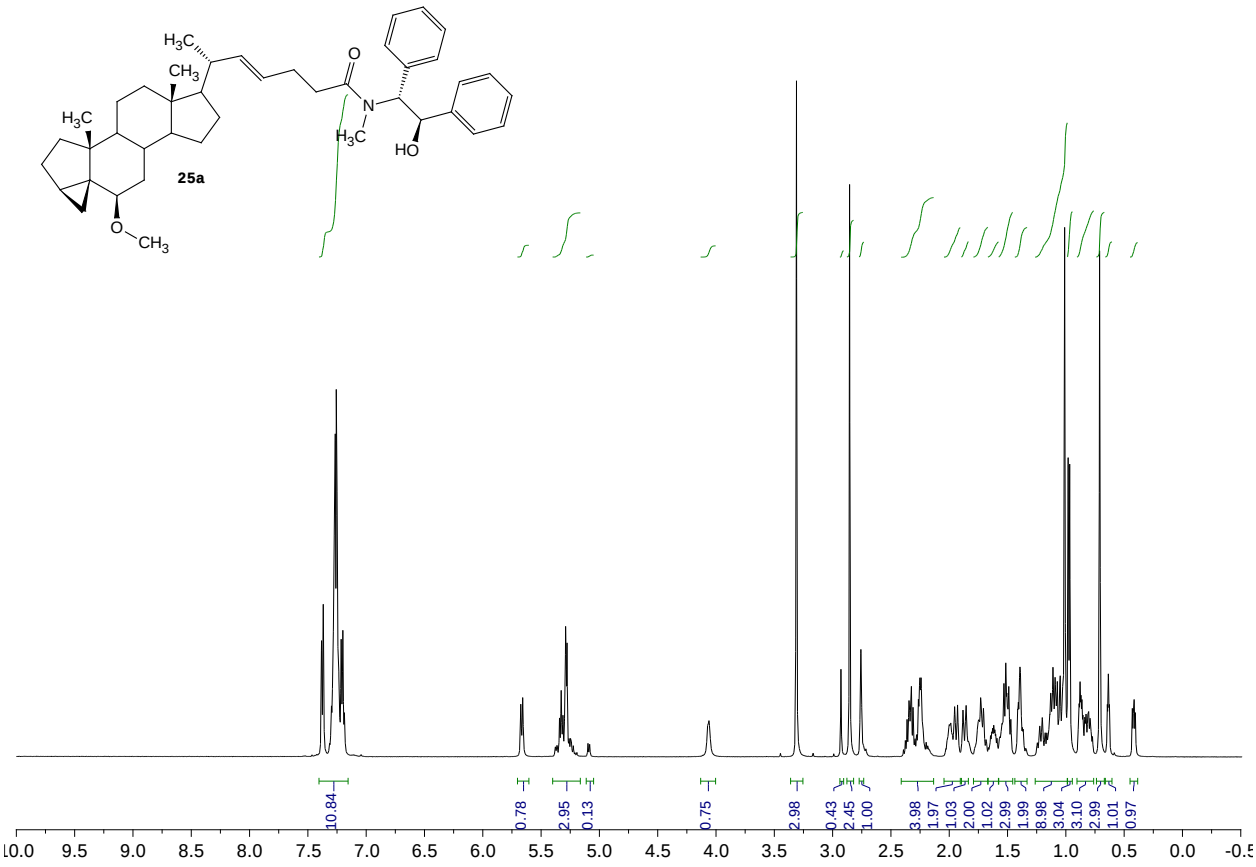
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1.03
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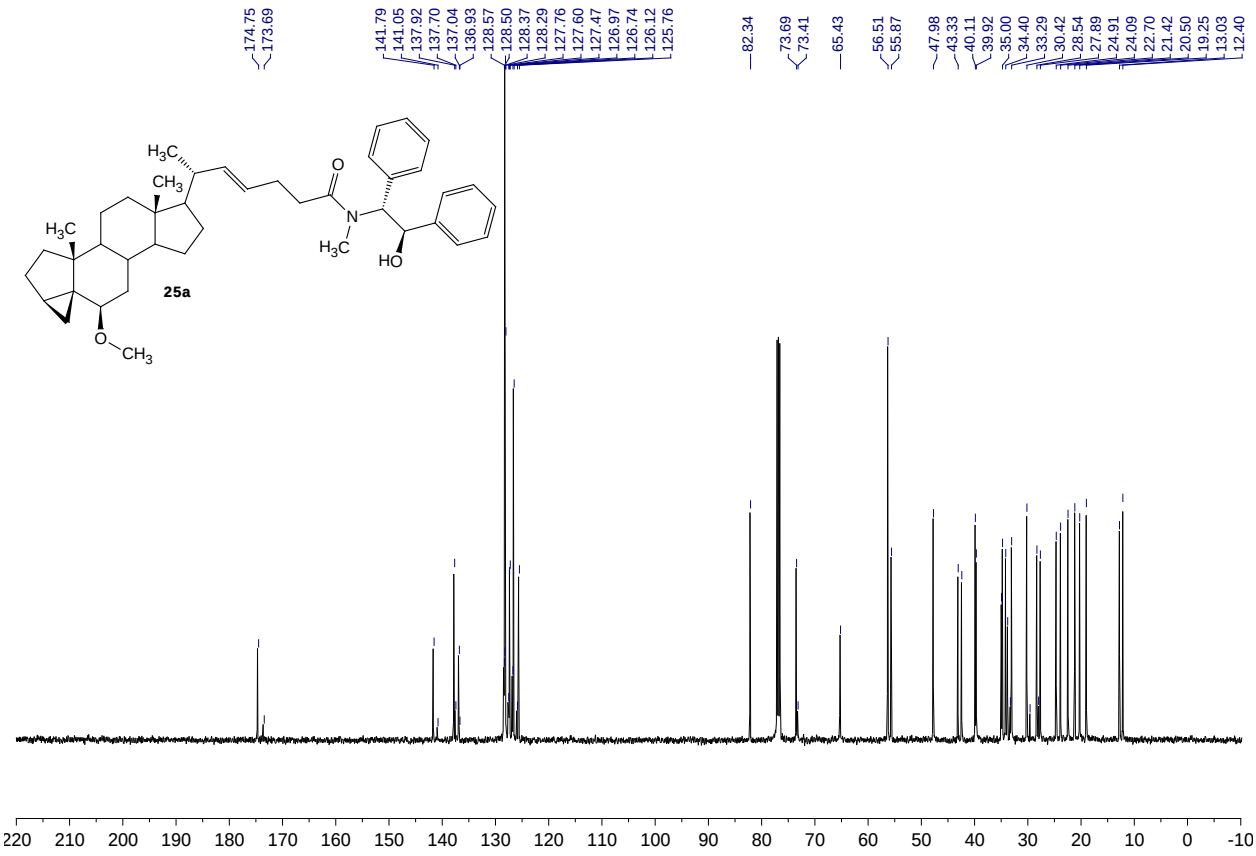
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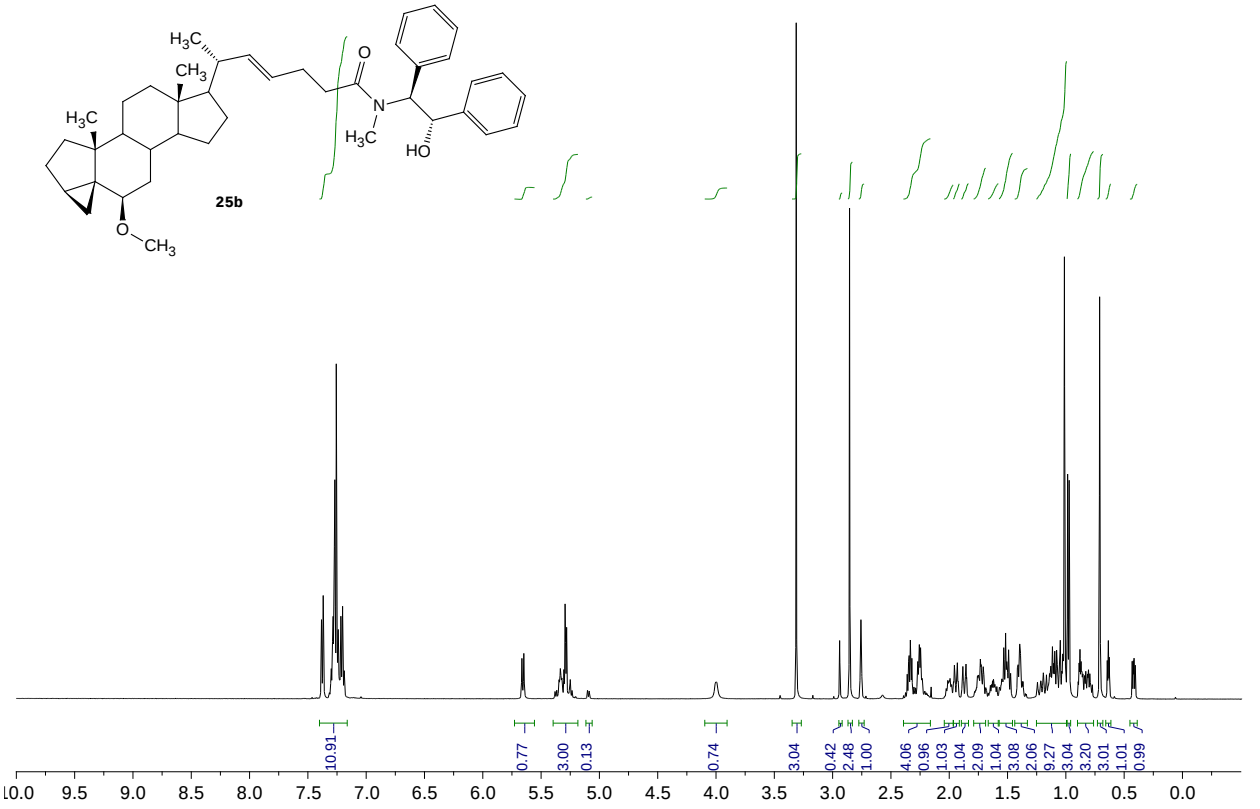
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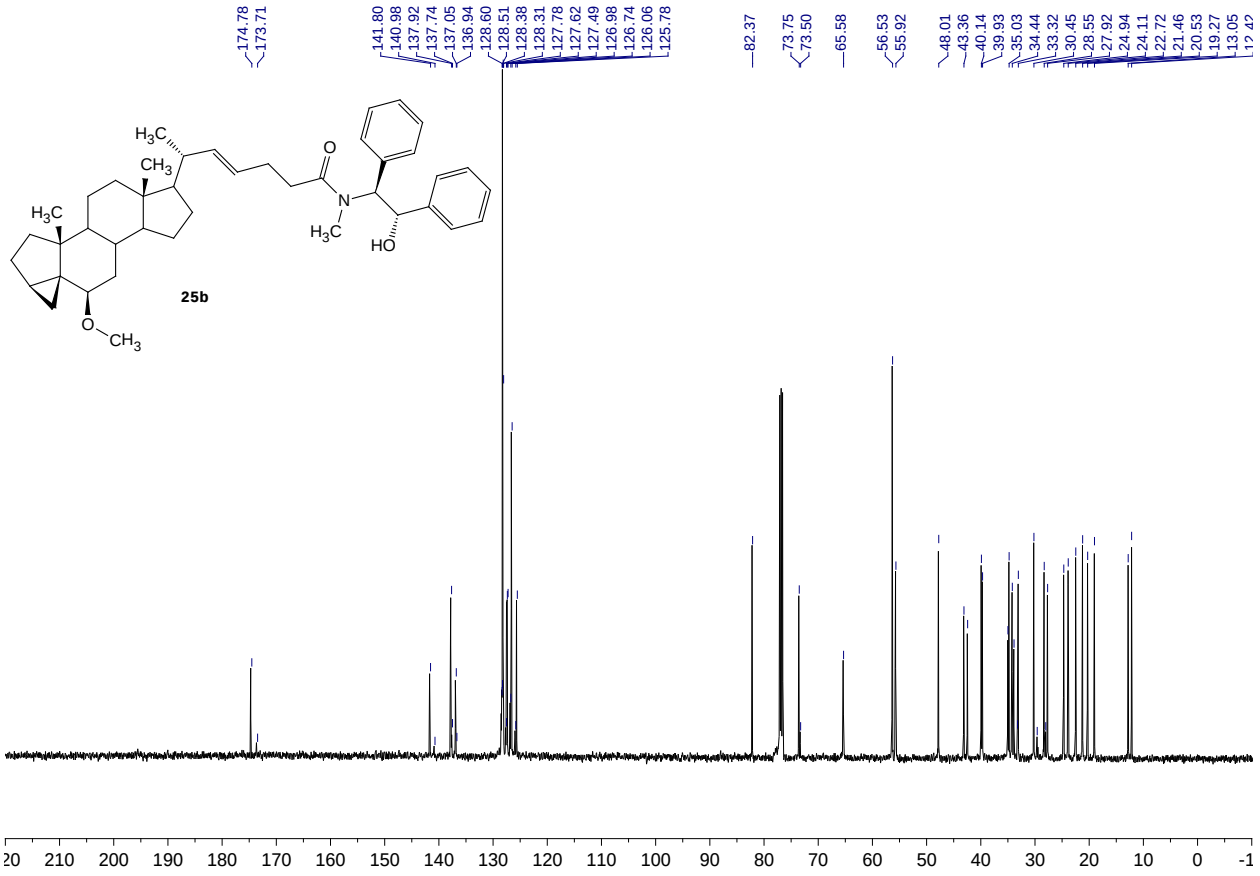
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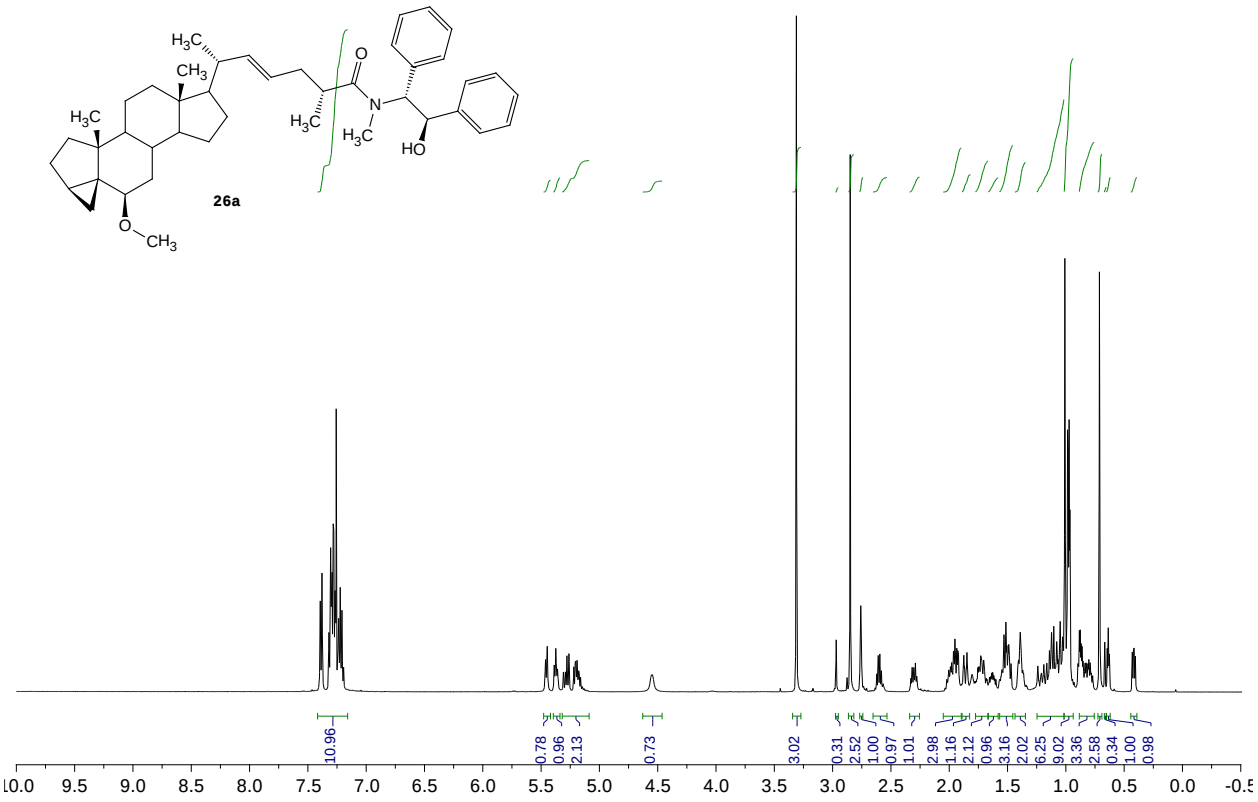
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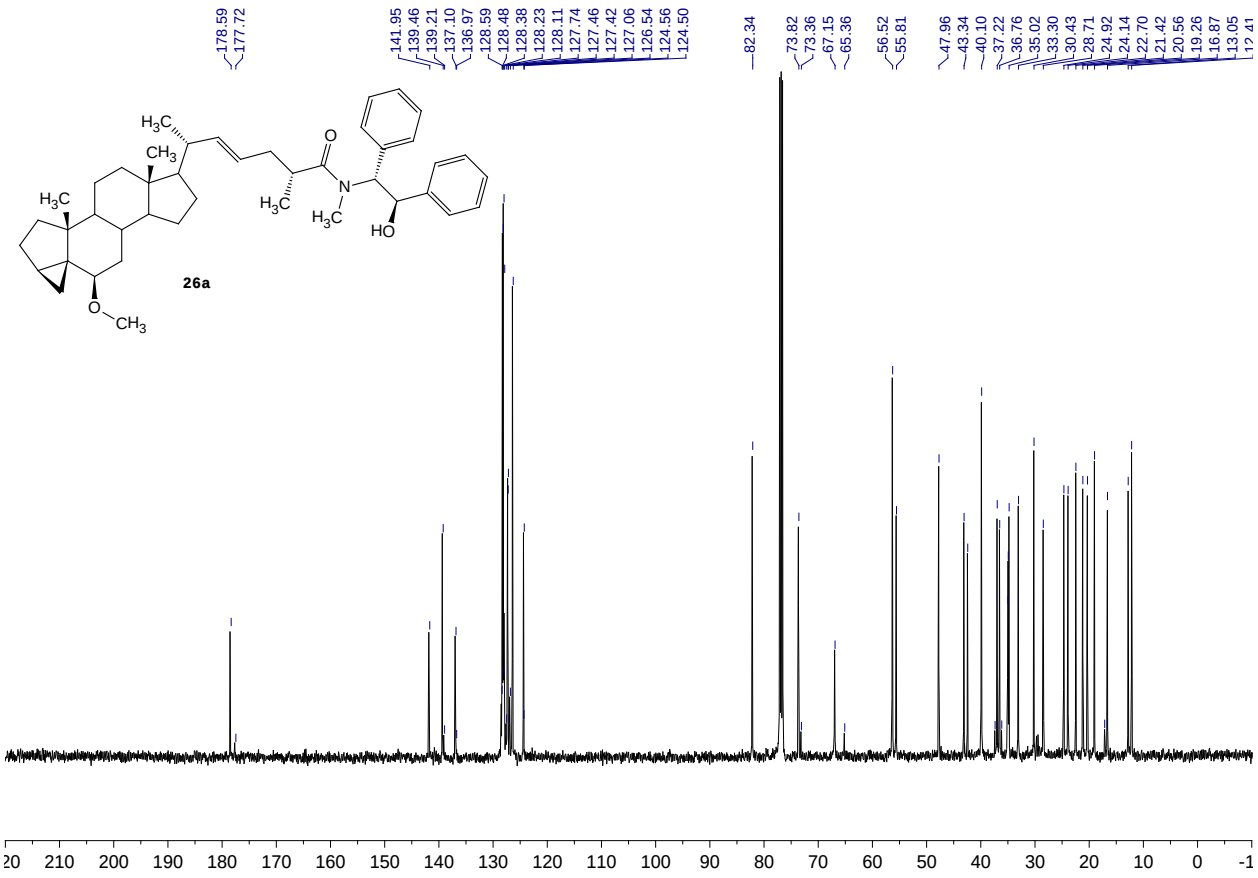
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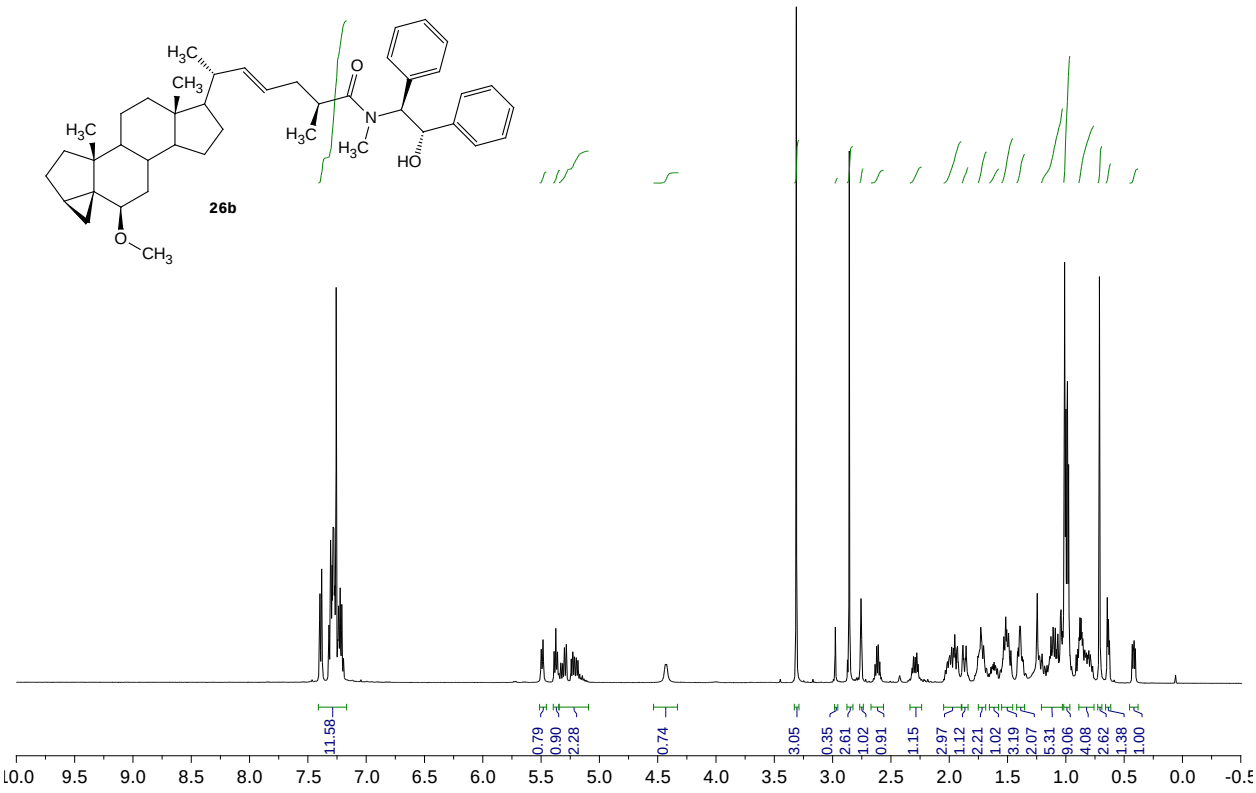
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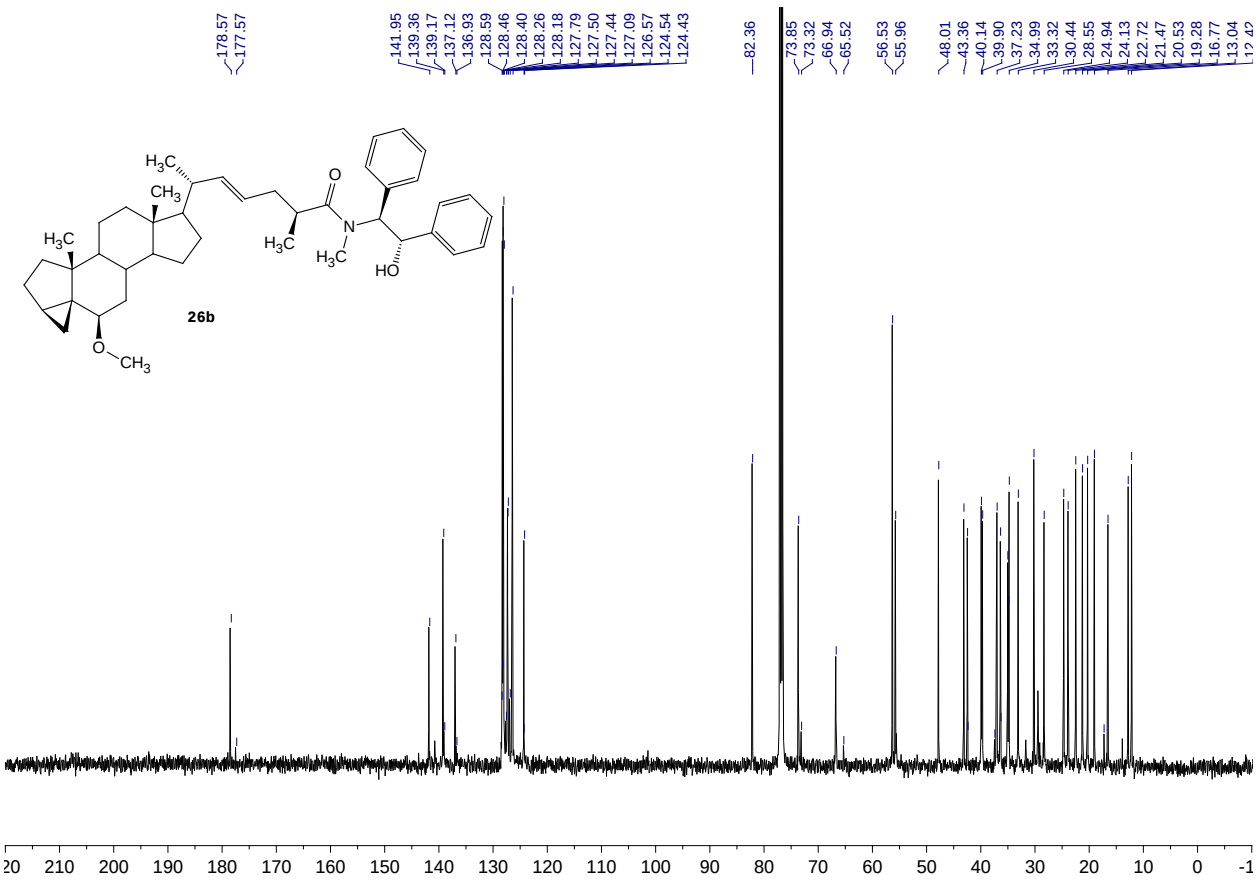
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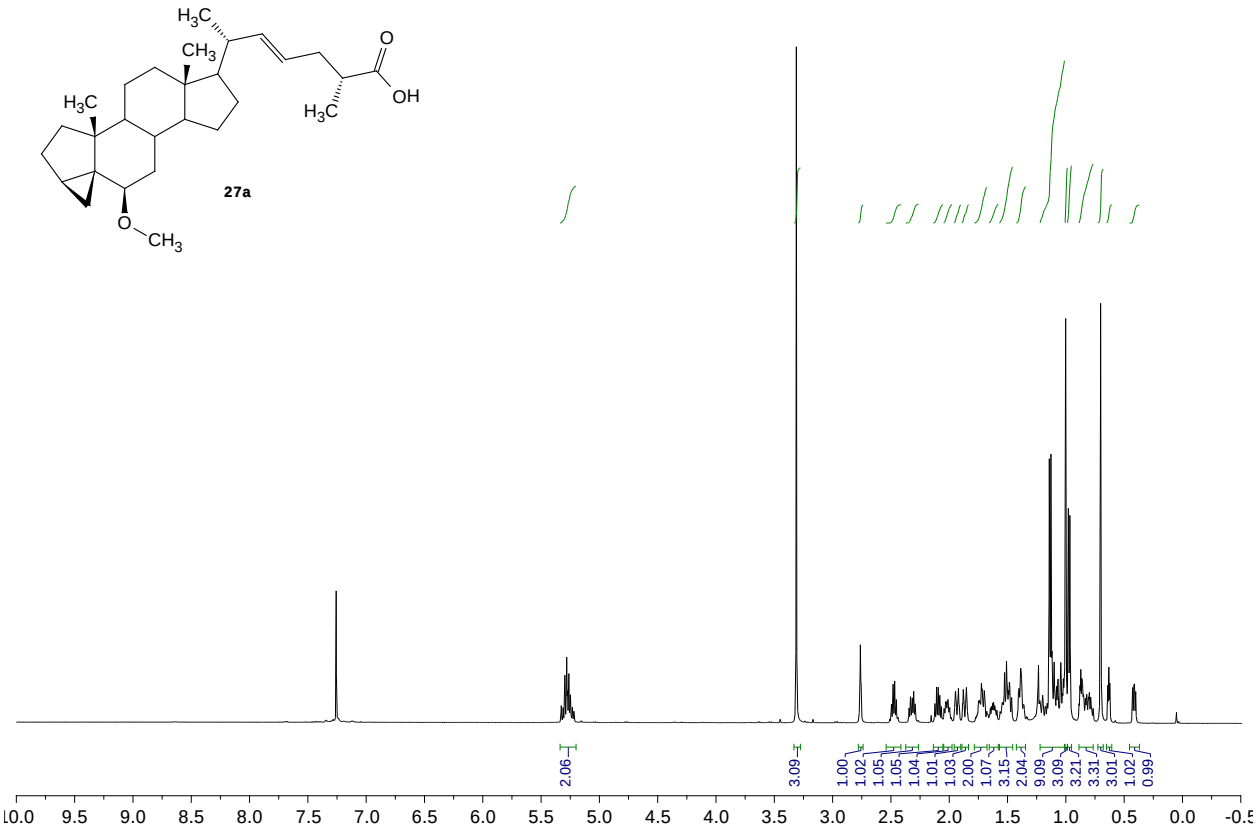
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1.04
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1.07
3.15
2.04
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3.01
1.02
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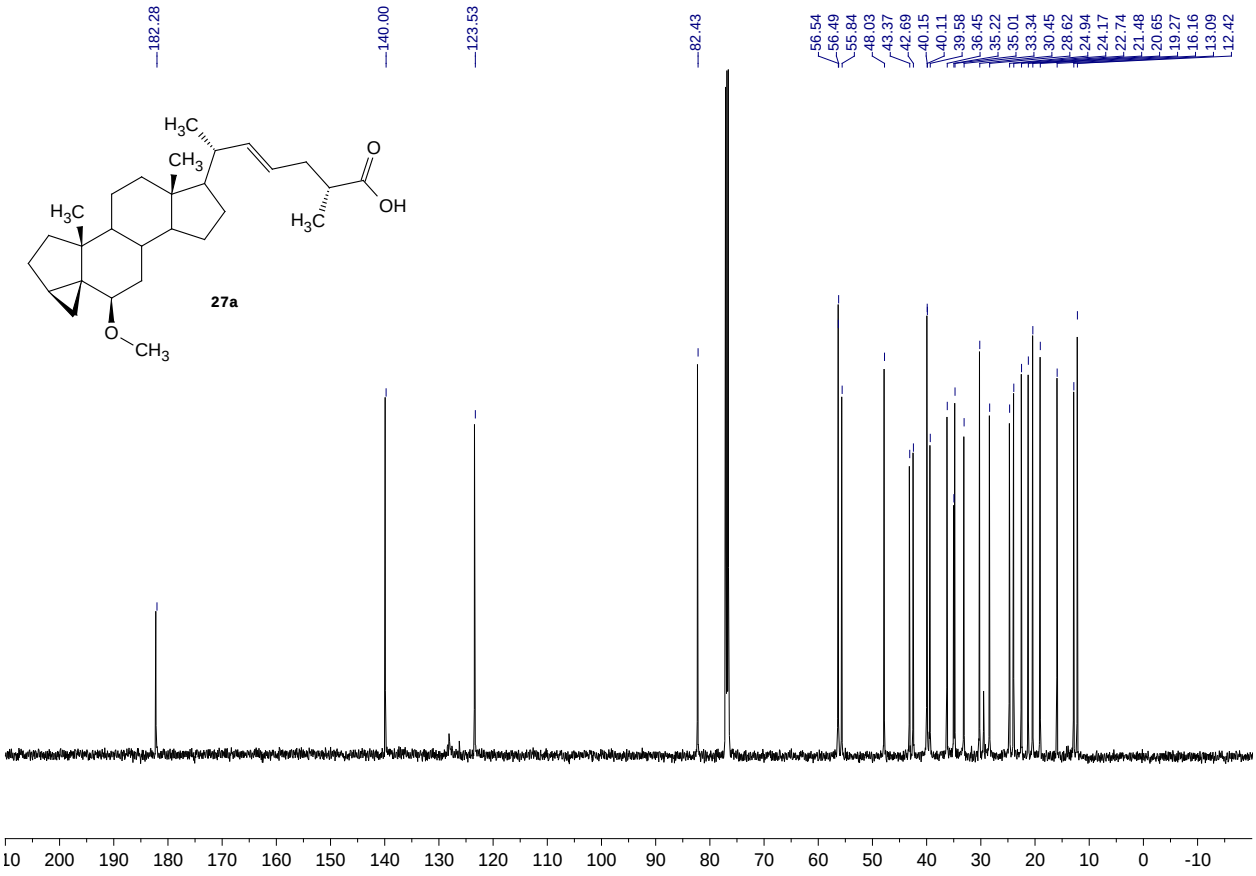
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48.03
43.37
42.69
40.15
40.11
39.58
36.45
35.22
35.01
33.34
30.45
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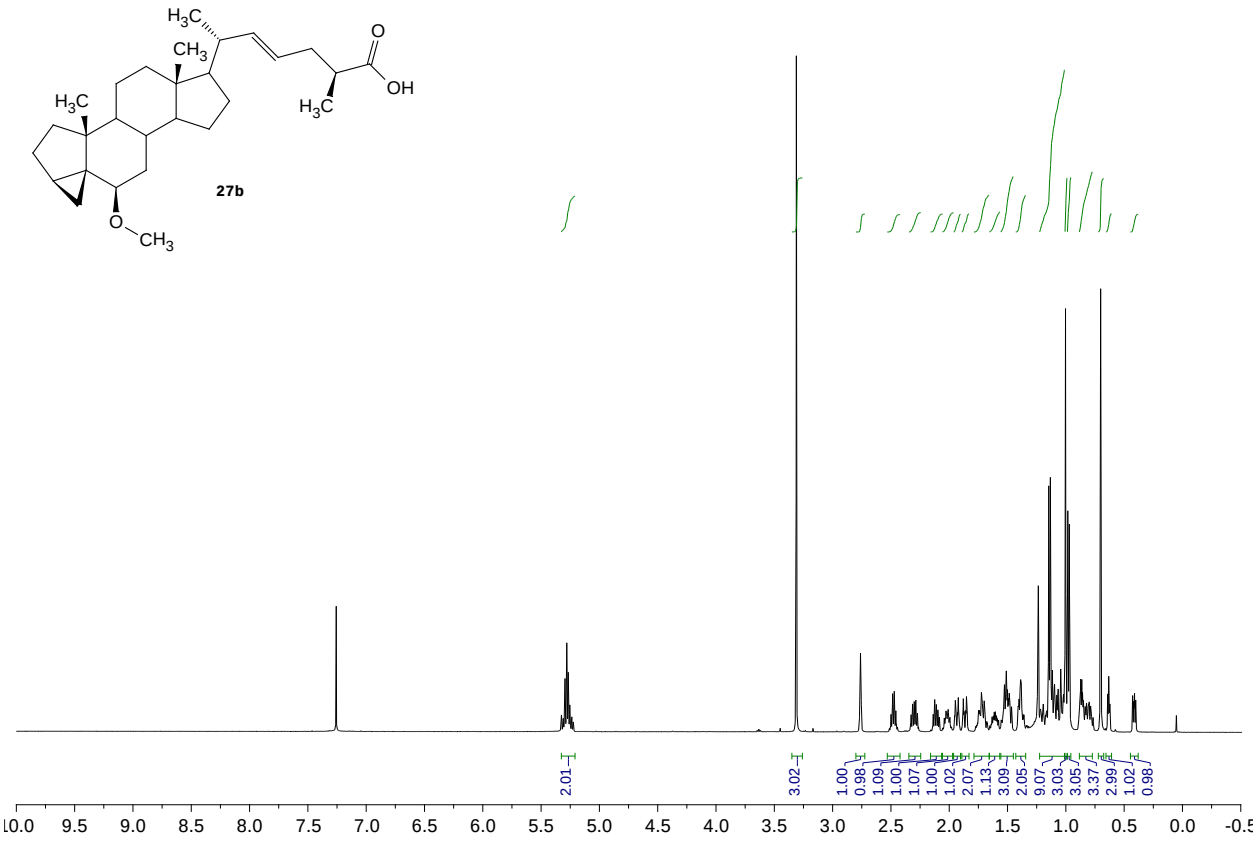
24.94
24.17
22.74
21.48
20.65
19.27
16.16
13.09
12.42
27a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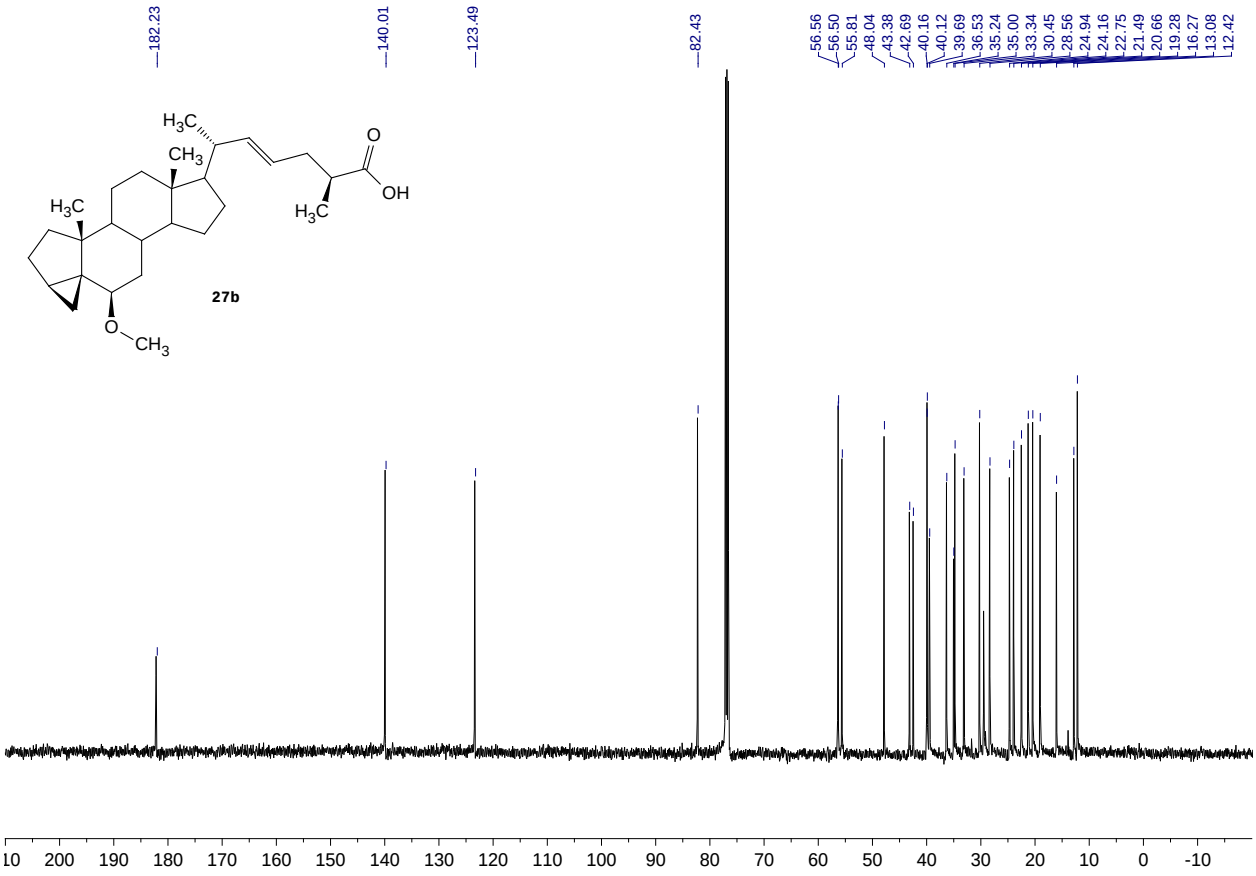
CH3
H3C
O
OH
H3C
27b
O
CH3
2.01
3.02
1.00
0.98
1.09
1.00
1.07
1.00
1.02
2.07
1.13
3.09
2.05
9.07
3.03
3.05
3.37
2.99
1.02
0.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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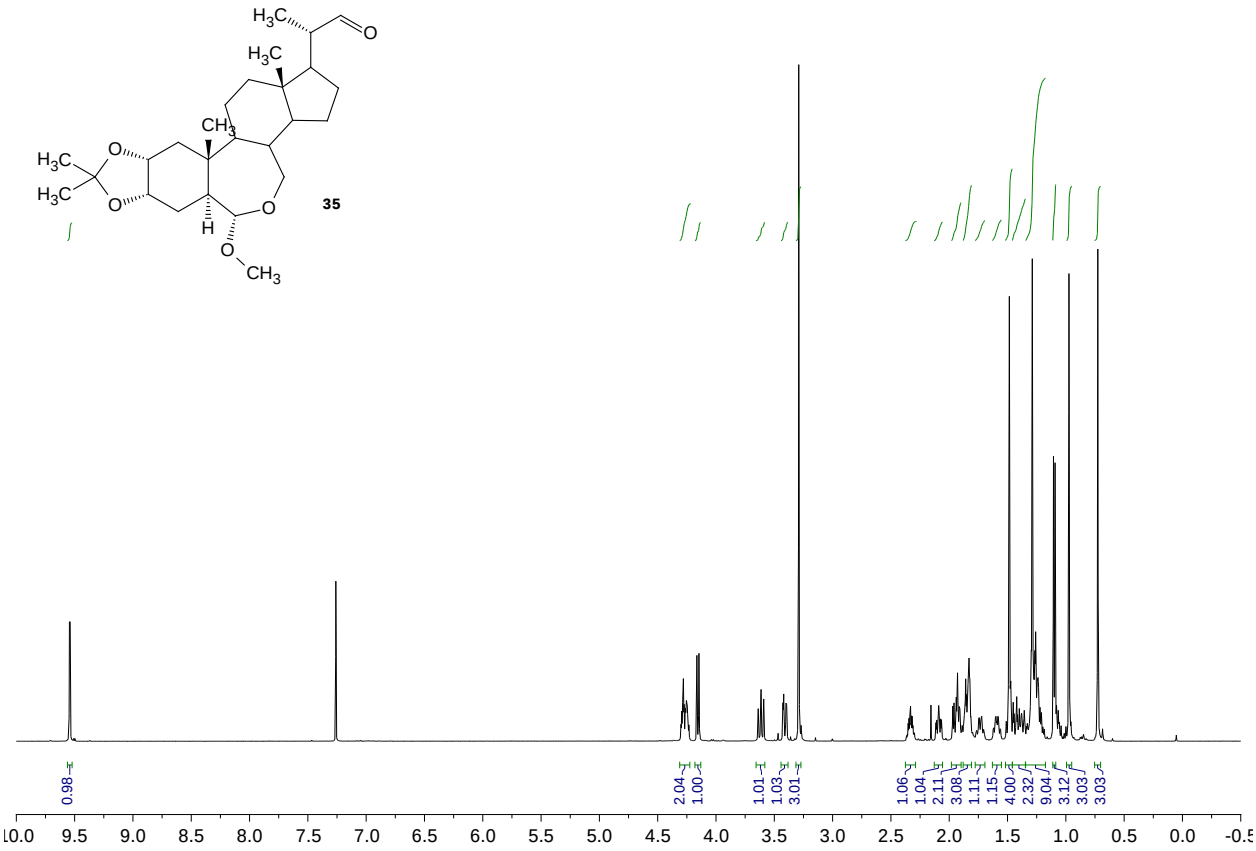
55.81
48.04
43.38
42.69
40.16
40.12
39.69
36.53
35.24
35.00
33.34
30.45
28.56
24.94
24.16
22.75
21.49
20.66
19.28
16.27
13.08
12.42
H3C
CH3
H3C
O
OH
H3C
27b
O
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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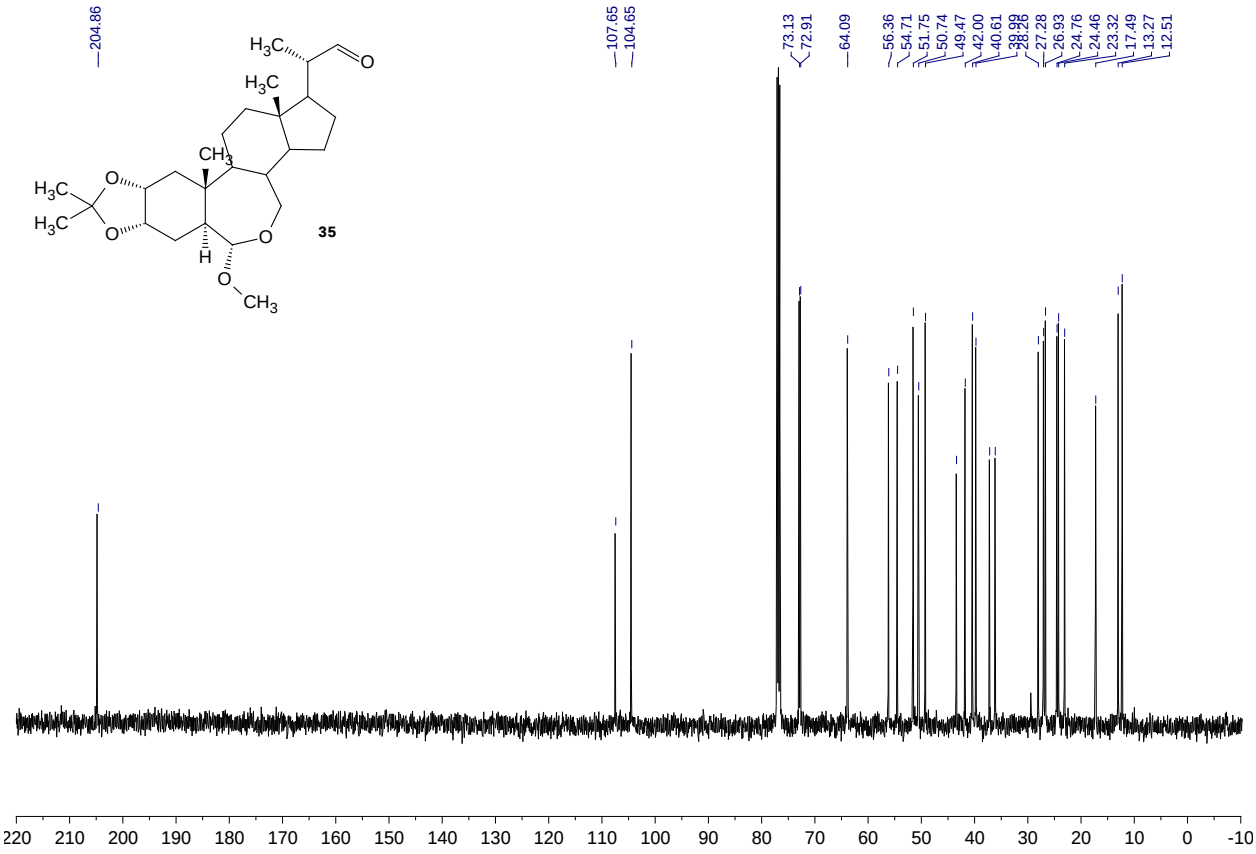
1.01
1.03
3.01
1.06
1.04
2.11
3.08
1.11
1.15
4.00
2.32
9.04
3.12
3.03
3.03


35
204.86
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104.65
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72.91
64.09
56.36
54.71
51.75
50.74
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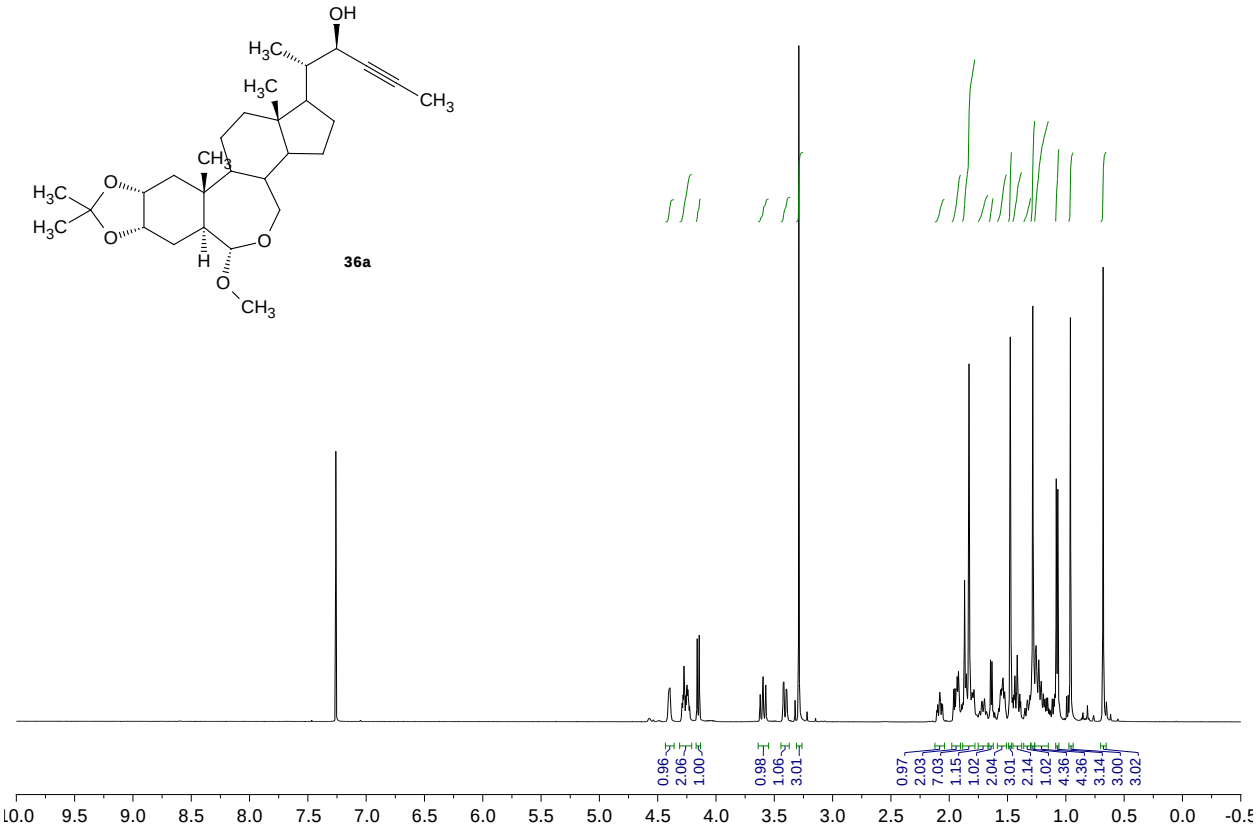
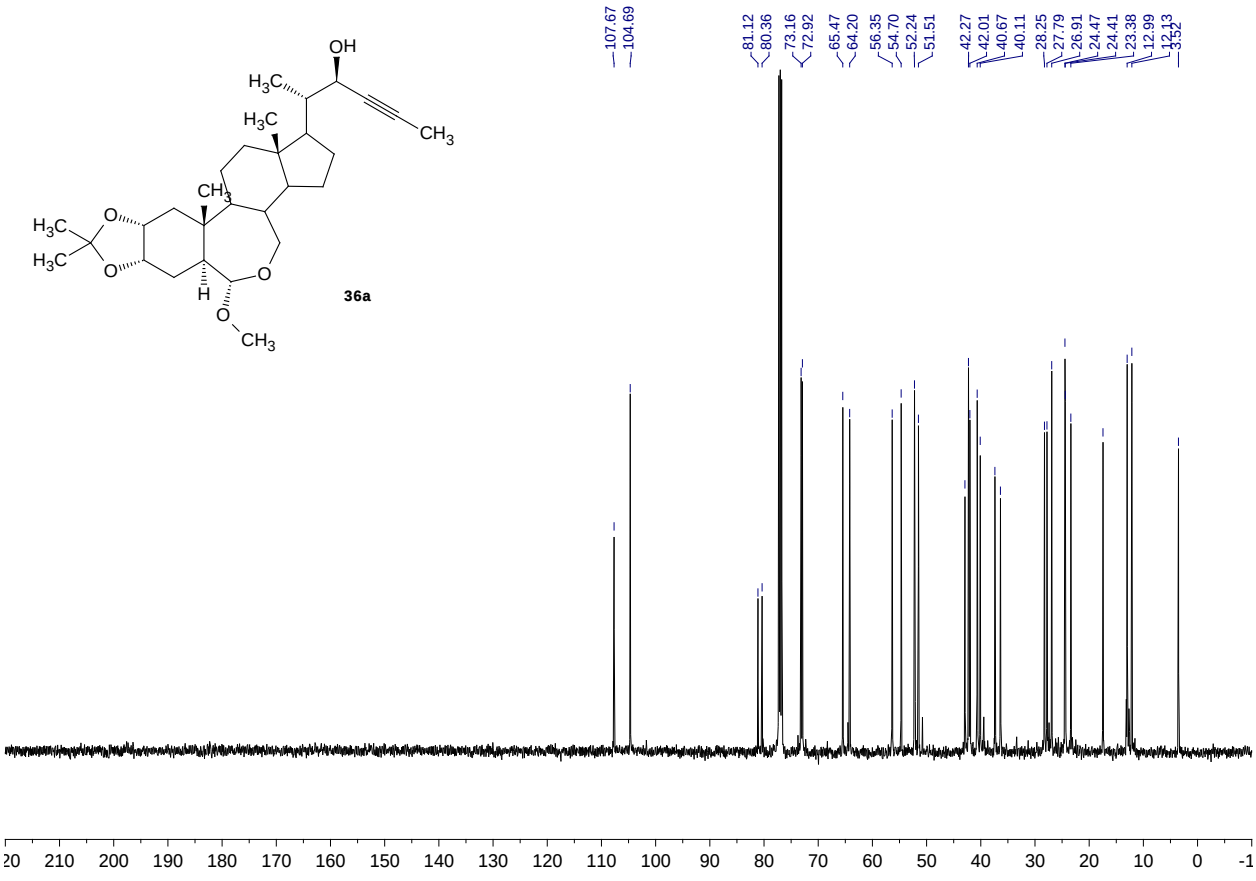
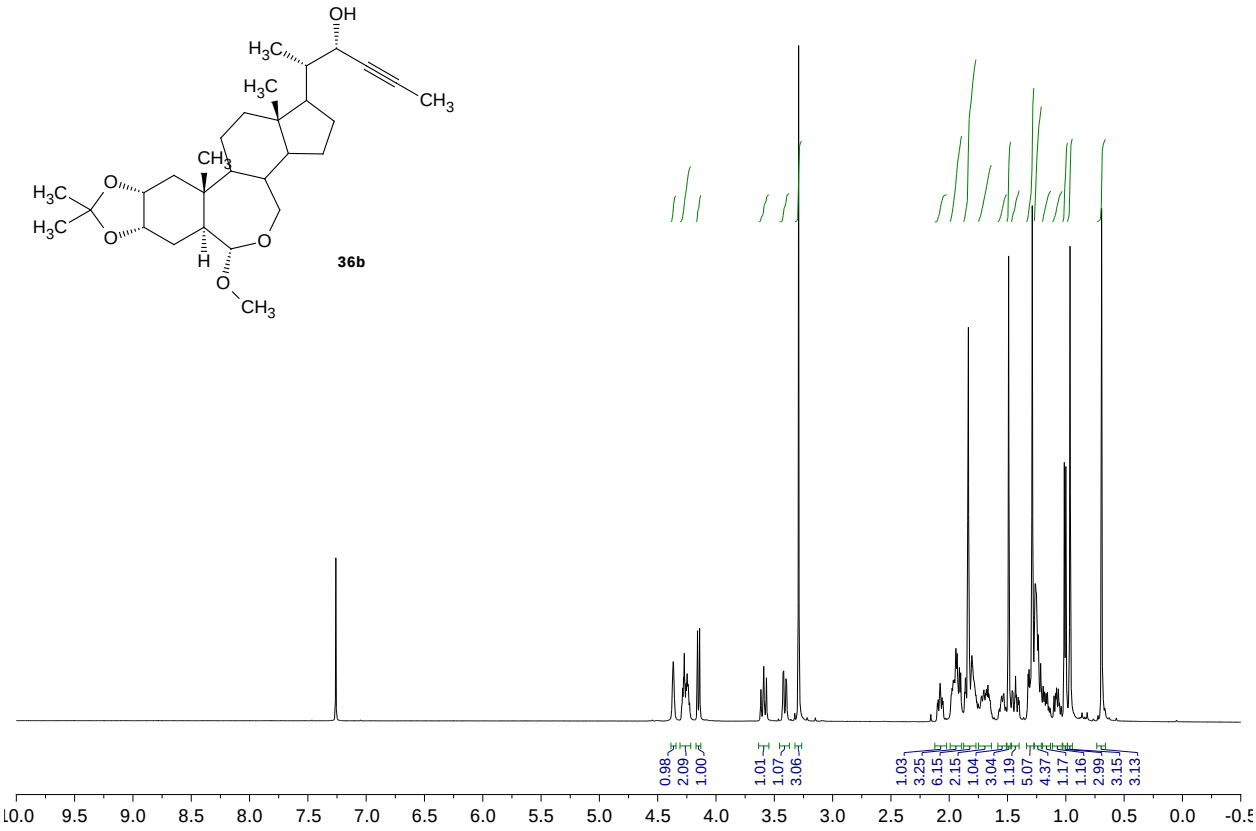
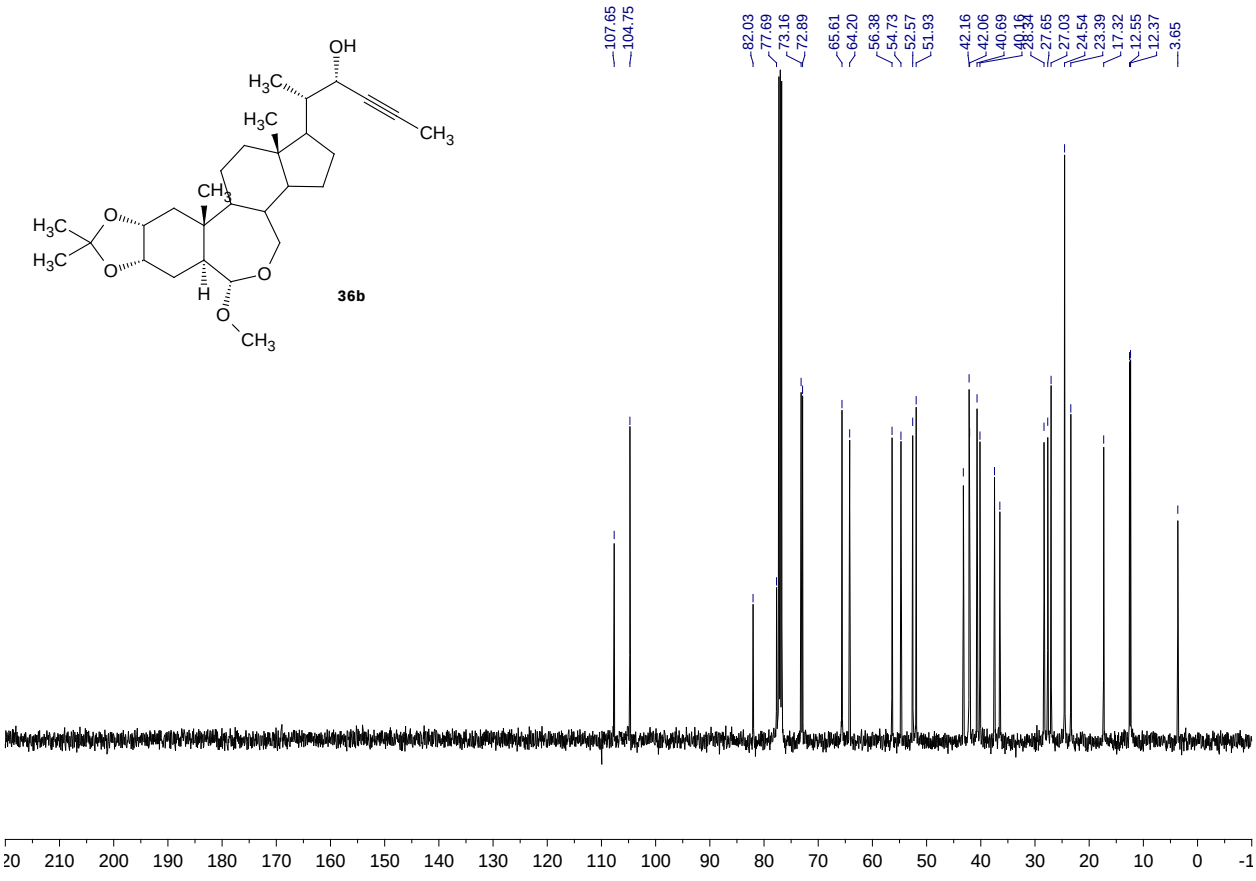
24.76
24.46
23.32
17.49
13.27
12.51


OH
H3C
H3C
CH3
CH3
H3C
H3C
O
O
O
H
O
CH3
36a
0.96
2.06
1.00
0.98
1.06
3.01
0.97
2.03
7.03
1.15
1.02
2.04
3.01
2.14
1.02
4.36
4.36
3.14
3.00
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


OH
H3C
H3C
CH3
CH3
H3C
H3C
O
O
O
H
O
CH3
36a
107.67
104.69
81.12
80.36
73.16
72.92
65.47
64.20
56.35
54.70
52.24
51.51
42.27
42.01
40.67
40.11
28.25
27.79
26.91
24.47
24.41
23.38
12.99
12.23
9.52
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


OH
H3C
H3C
CH3
CH3
H3C
H3C
O
O
O
H
O
CH3
36b
0.98
2.09
1.00
1.01
1.07
3.06
1.03
3.25
6.15
2.15
1.04
3.04
1.19
5.07
4.37
1.17
1.16
2.99
3.15
3.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0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H3C
H3C
CH3
CH3
H3C
H3C
O
O
O
H
O
CH3
36b
107.65
104.75
82.03
77.69
73.16
72.89
65.61
64.20
56.38
54.73
52.57
51.93
42.16
42.06
40.69
27.65
27.03
24.54
23.39
17.32
12.55
12.37
3.65
210
200
190
180
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150
140
130
120
110
100
90
80
70
60
50
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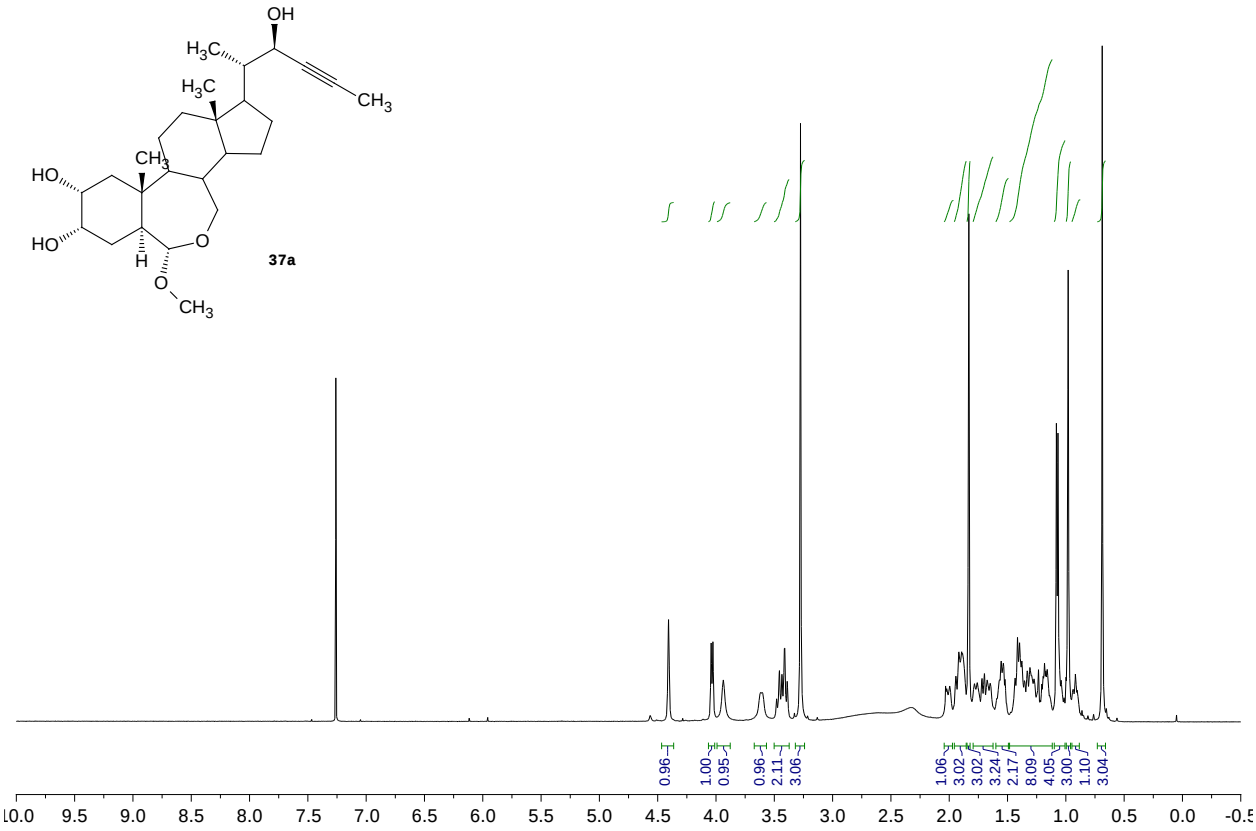
30
20
10
0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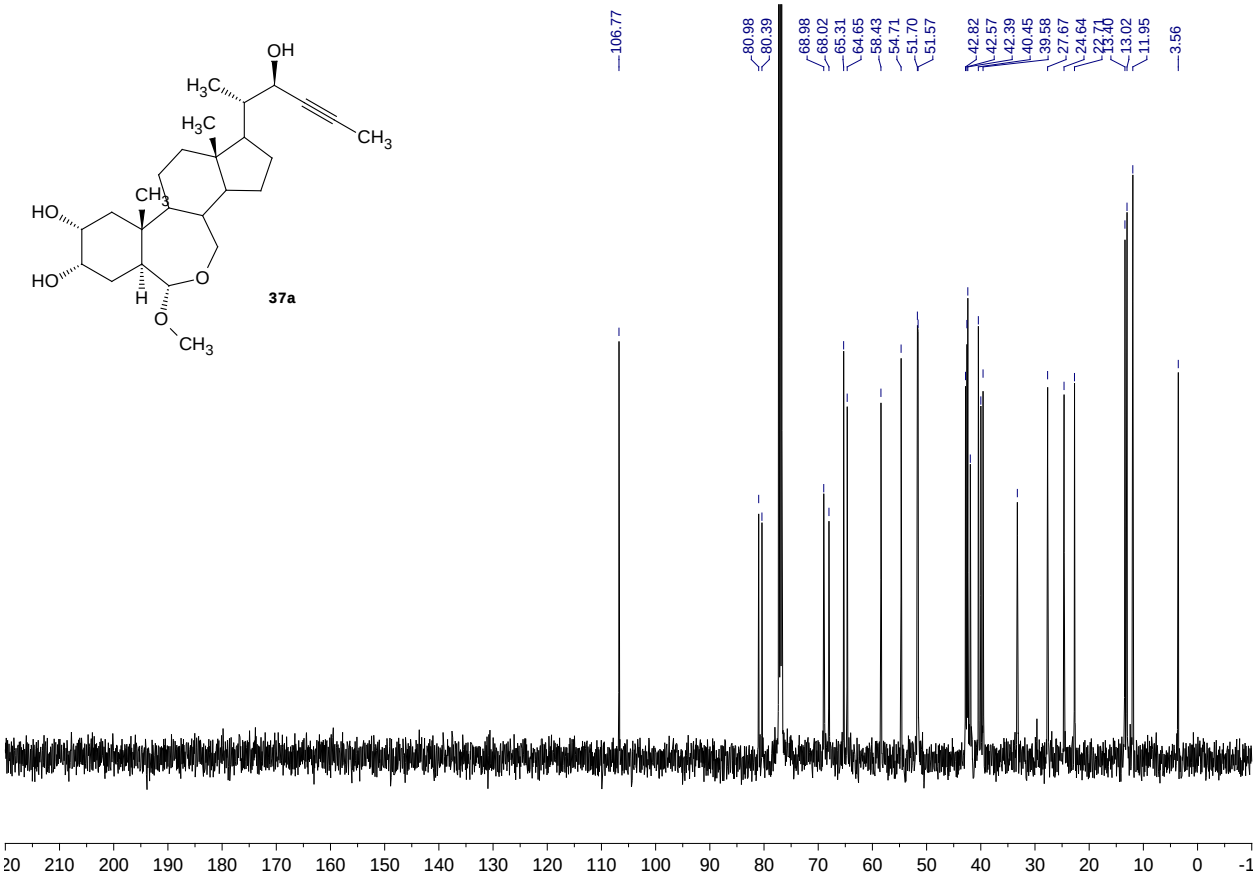
H3C
H3C
CH3
CH3
HO
HO
H
O
O
CH3
37a
0.96
1.00
0.95
0.96
2.11
3.06
1.06
3.02
3.02
3.24
2.17
8.09
4.05
3.00
1.10
3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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H3C
H3C
CH3
CH3
HO
HO
H
O
O
CH3
37a
106.77
80.98
80.39
68.98
68.02
65.31
64.65
58.43
54.71
51.70
51.57
42.82
42.57
42.39
40.45
39.58
27.67
24.64
13.40
13.02
11.95
3.56
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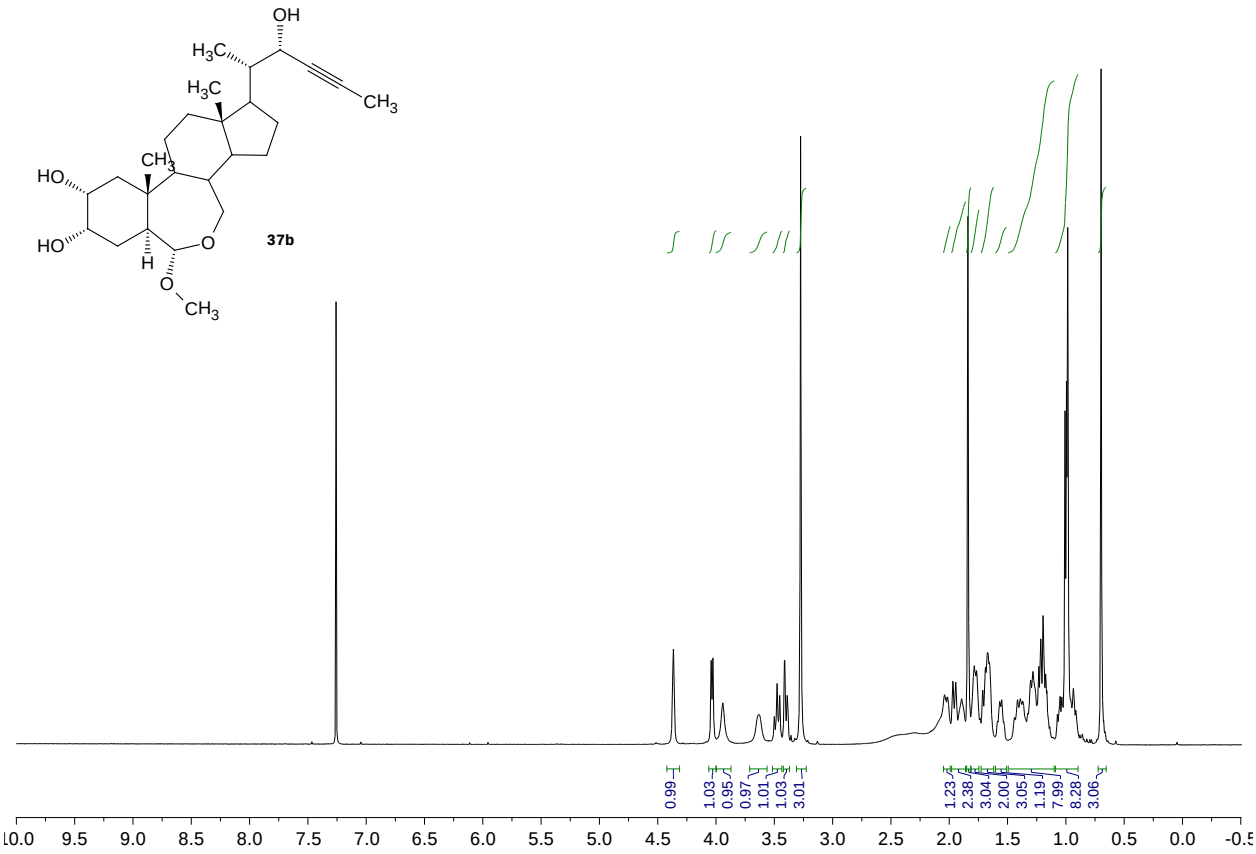
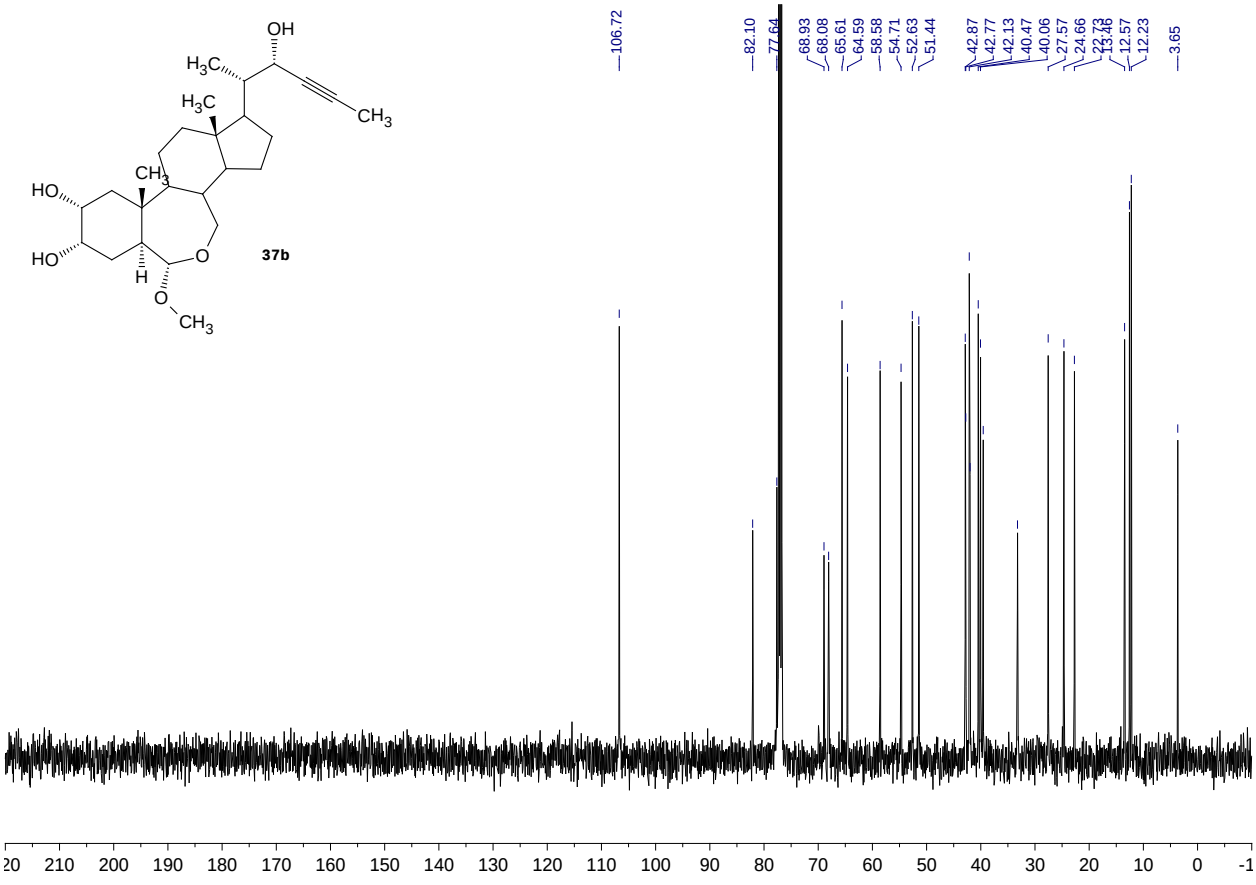
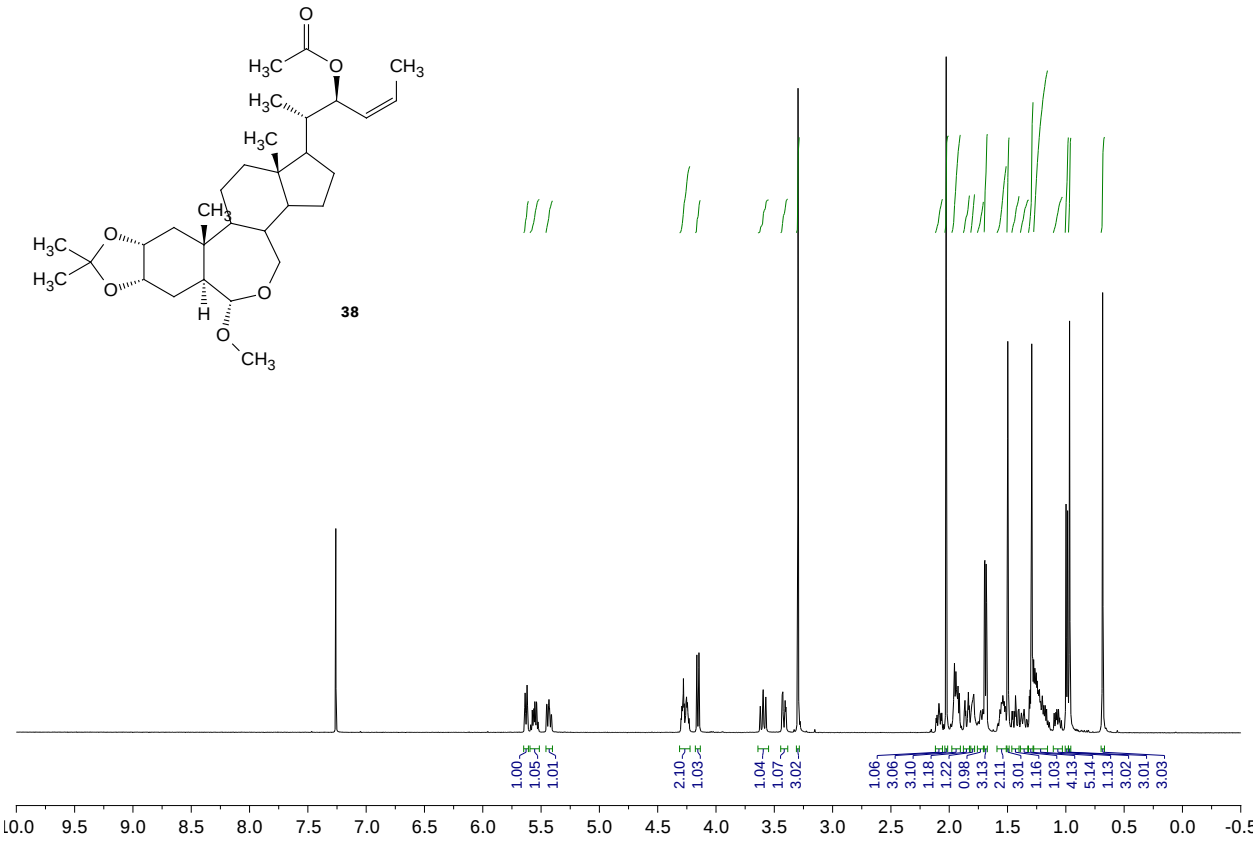

OH
H3C
H3C
CH3
CH3
HO
HO
O
H
O
CH3
37b
0.99
1.03
0.95
0.97
1.01
1.03
3.01
1.23
2.38
3.04
2.00
3.05
1.19
7.99
8.28
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


OH
H3C
H3C
CH3
CH3
HO
HO
O
H
O
CH3
37b
106.72
82.10
77.64
68.93
68.08
65.61
64.59
58.58
54.71
52.63
51.44
42.87
42.77
42.13
40.47
40.06
27.57
24.66
12.57
12.23
3.65
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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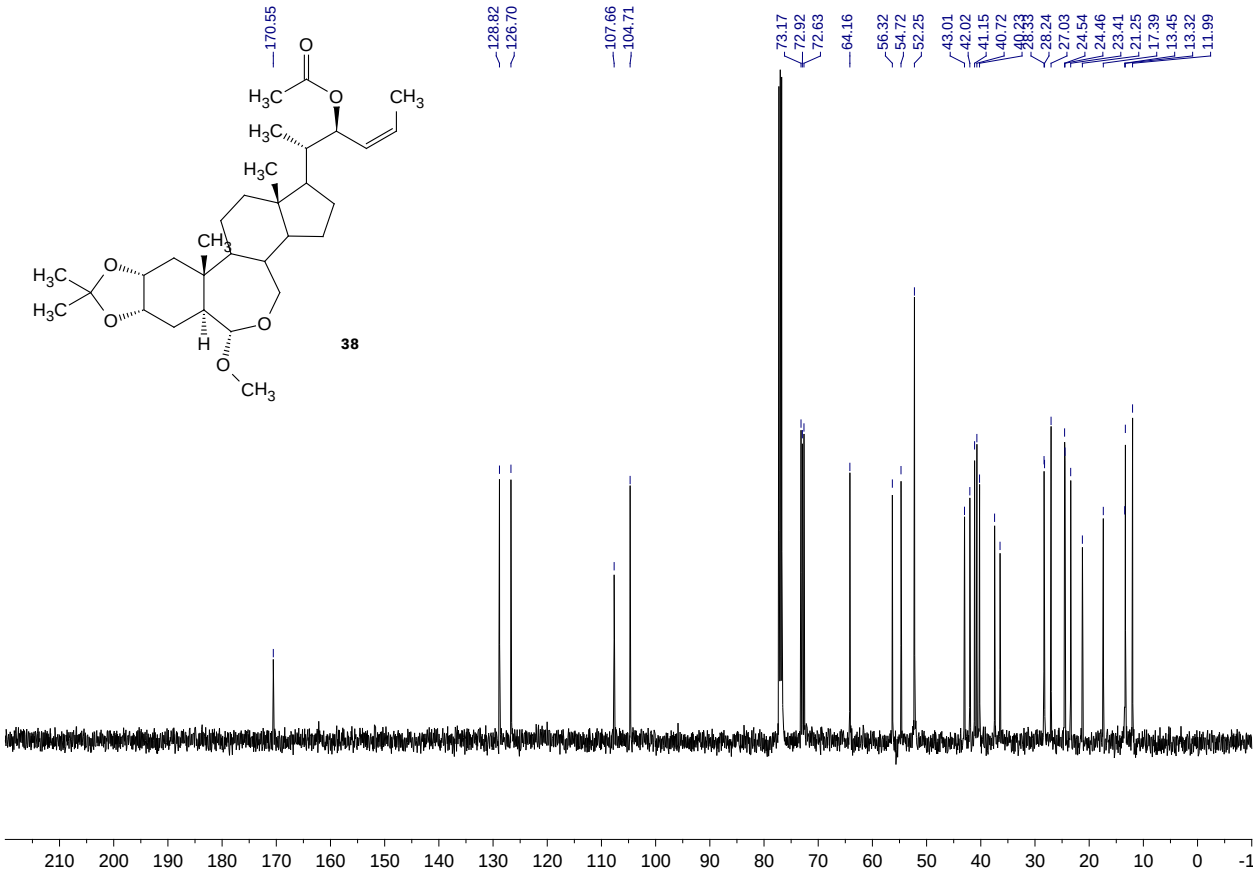
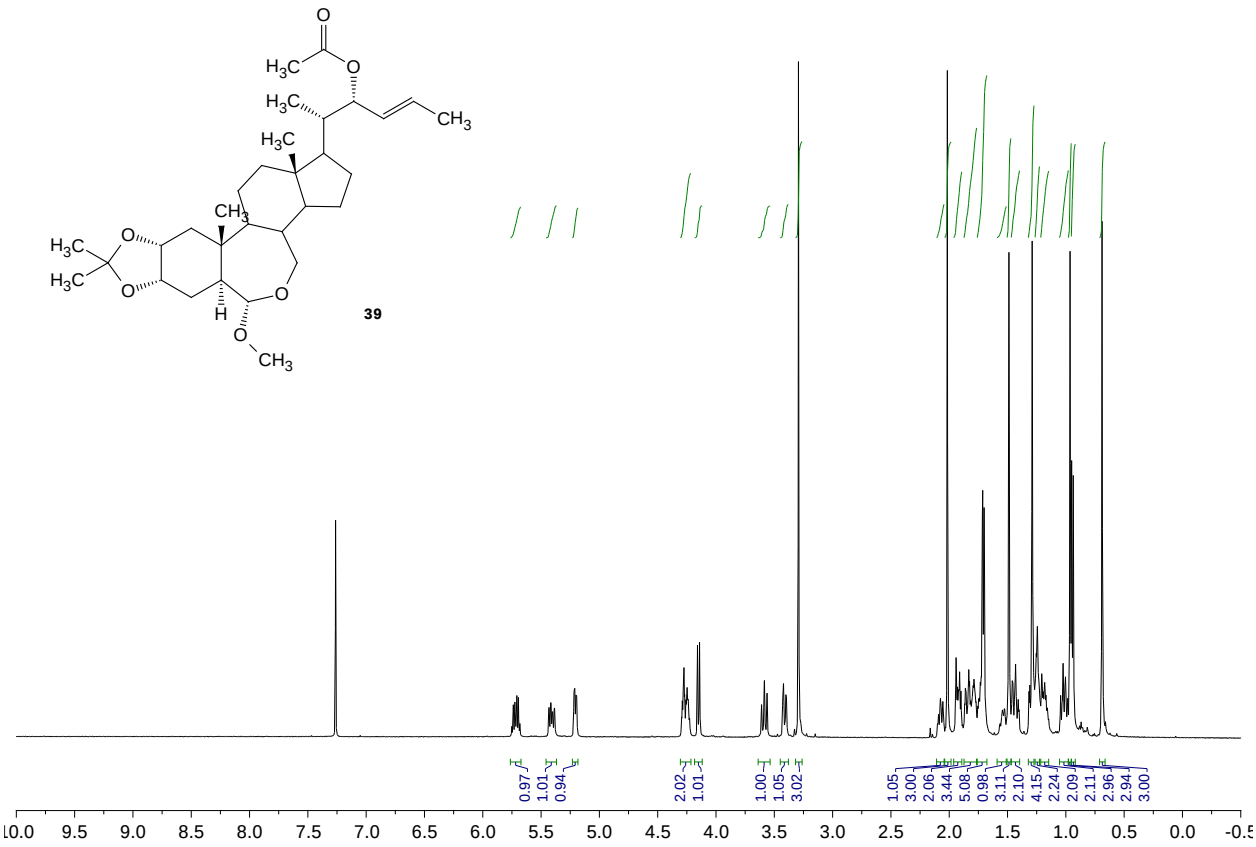

38


39
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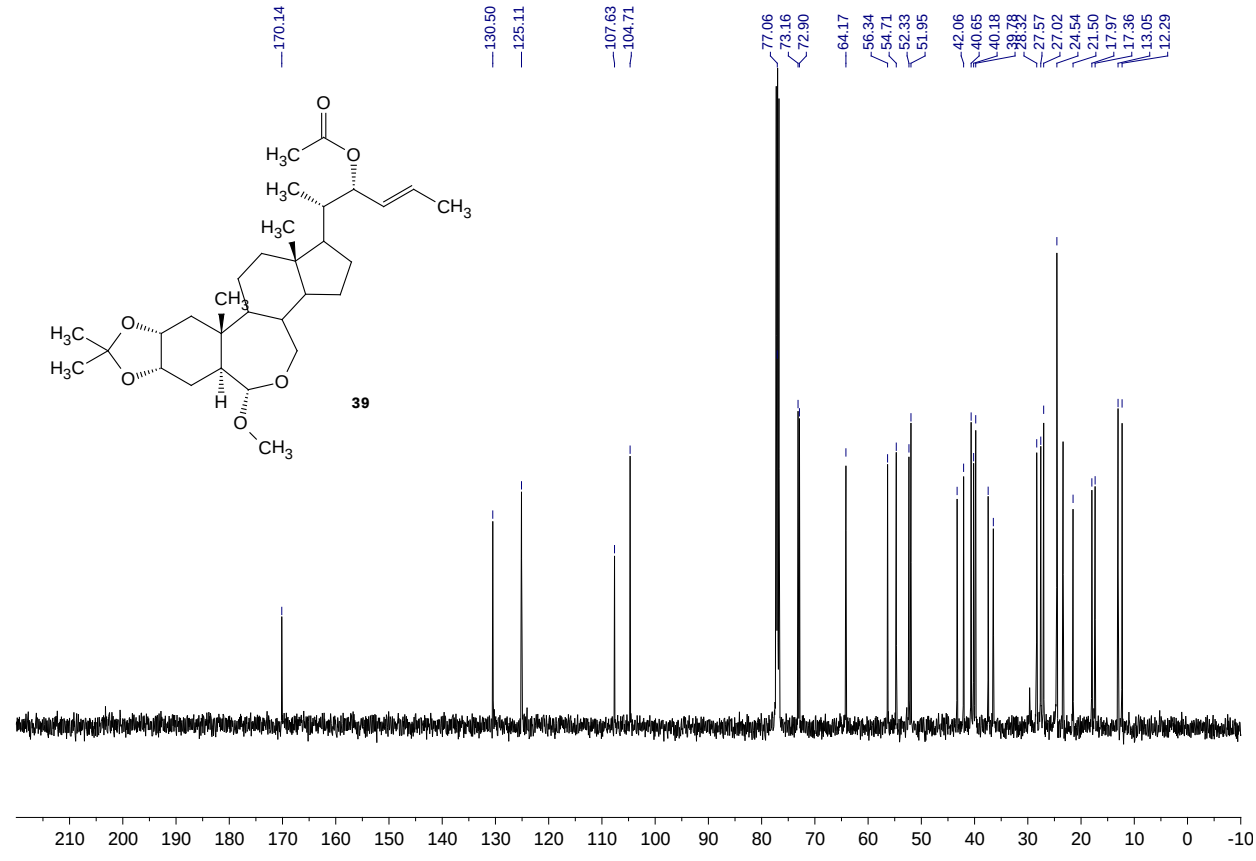
1.01
0.94
2.02
1.01
1.00
1.05
3.02
1.05
3.00
2.06
3.44
5.08
0.98
3.11
2.10
4.15
2.24
2.09
2.11
2.96
2.94
3.00


39
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130.50
125.11
107.63
104.71
77.06
73.16
72.90
64.17
56.34
54.71
52.33
51.95
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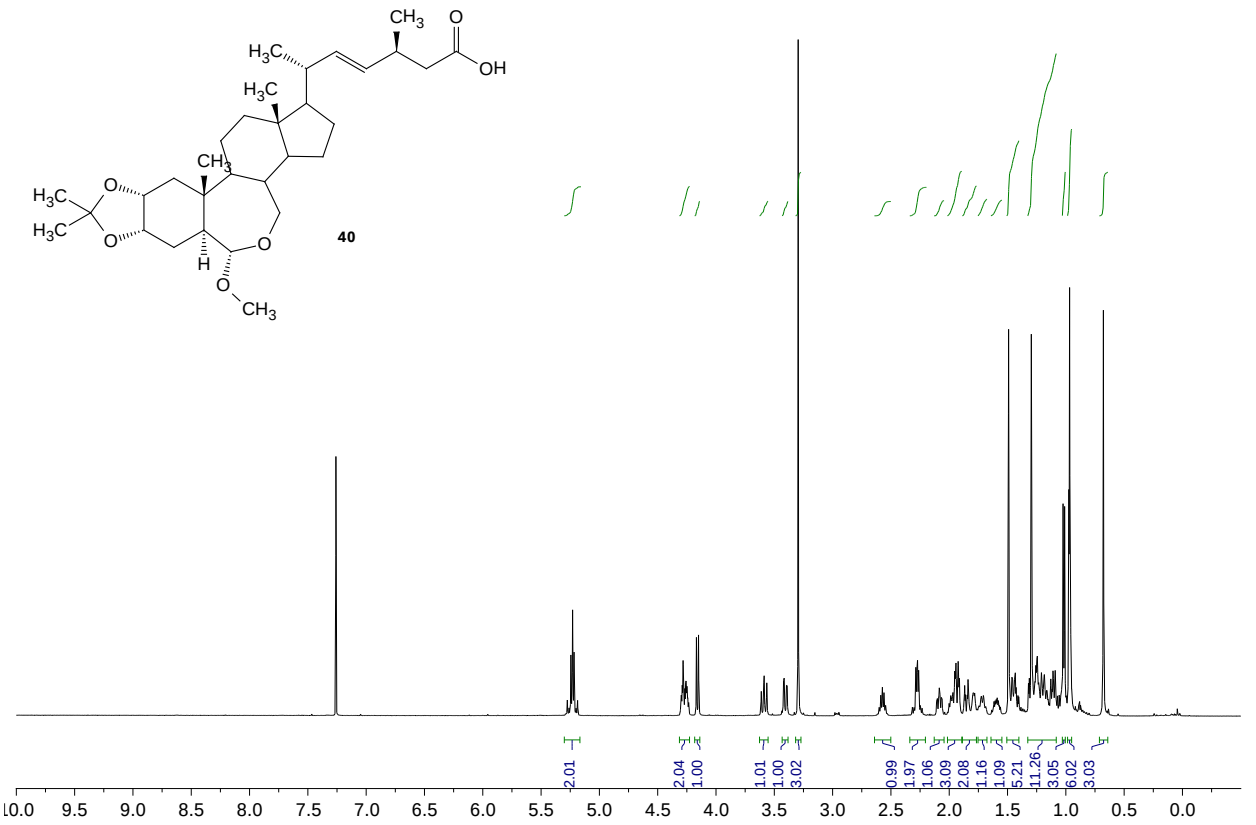
40.18
27.57
27.02
24.54
21.50
17.97
17.36
13.05
12.29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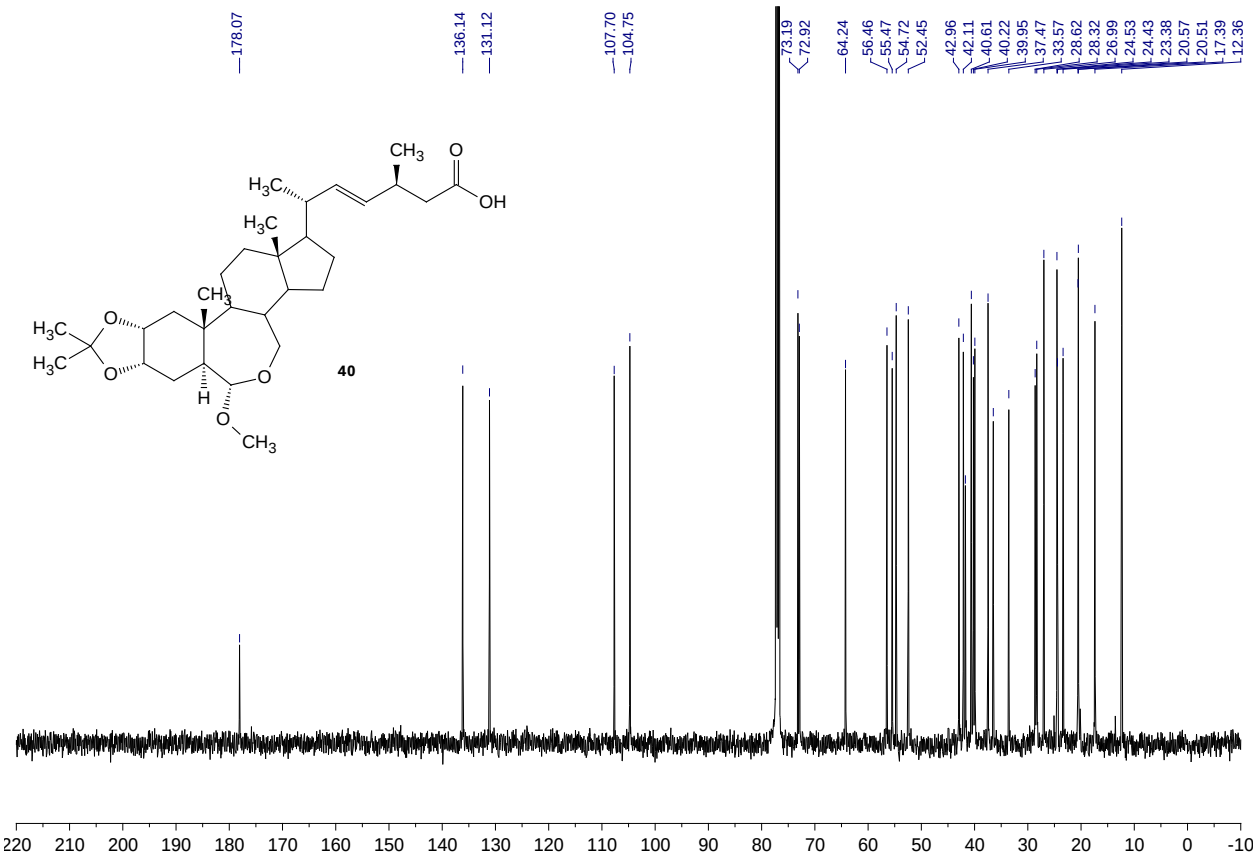
H3C
OH
H3C
CH3
H3C
O
H3C
O
O
H
O
CH3
40
2.01
2.04
1.00
1.01
1.00
3.02
0.99
1.97
1.06
3.09
2.08
1.16
1.09
5.21
11.26
3.05
6.02
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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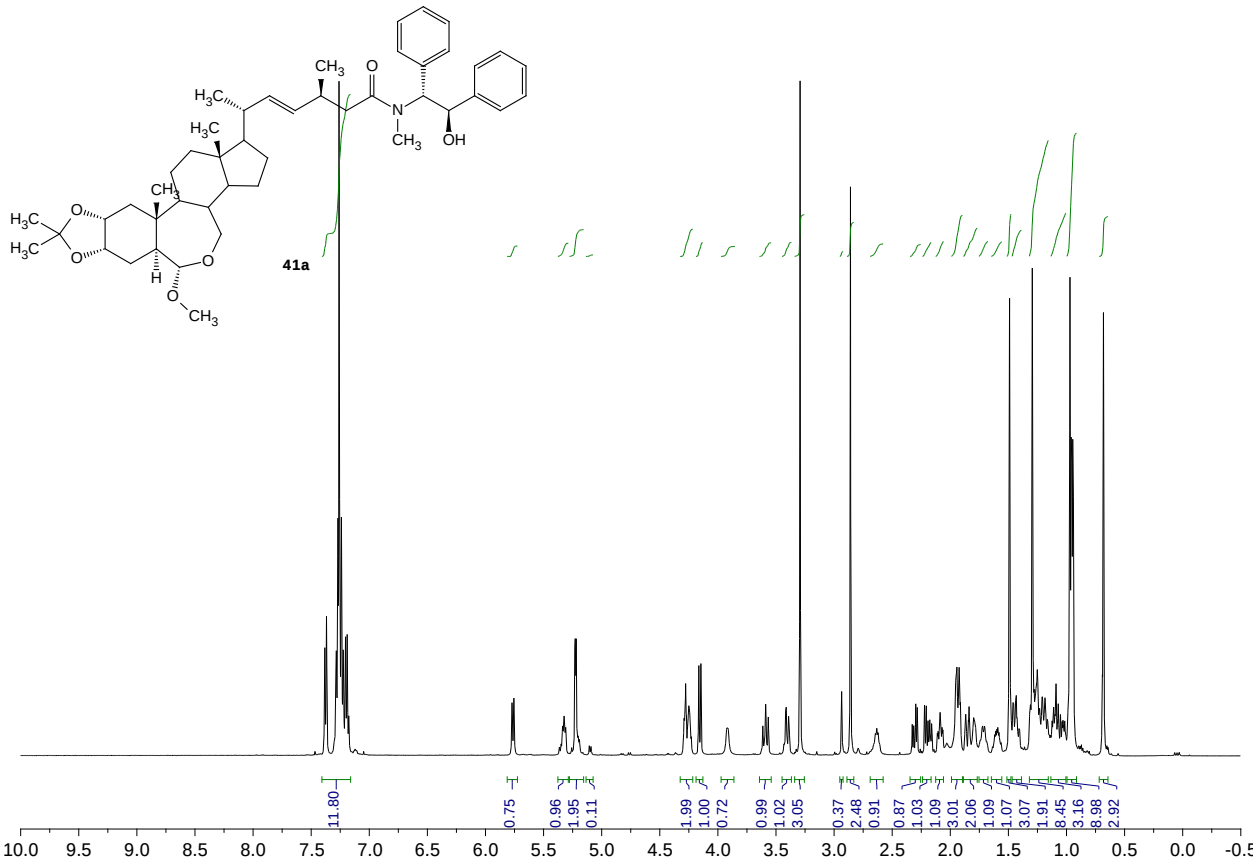
104.75
73.19
72.92
64.24
56.46
55.47
54.72
52.45
42.96
42.11
40.61
40.22
39.95
37.47
33.57
28.62
28.32
26.99
24.53
24.43
23.38
20.57
20.51
17.39
12.36
CH3
O
H3C
OH
H3C
CH3
H3C
O
H3C
O
O
H
O
CH3
40
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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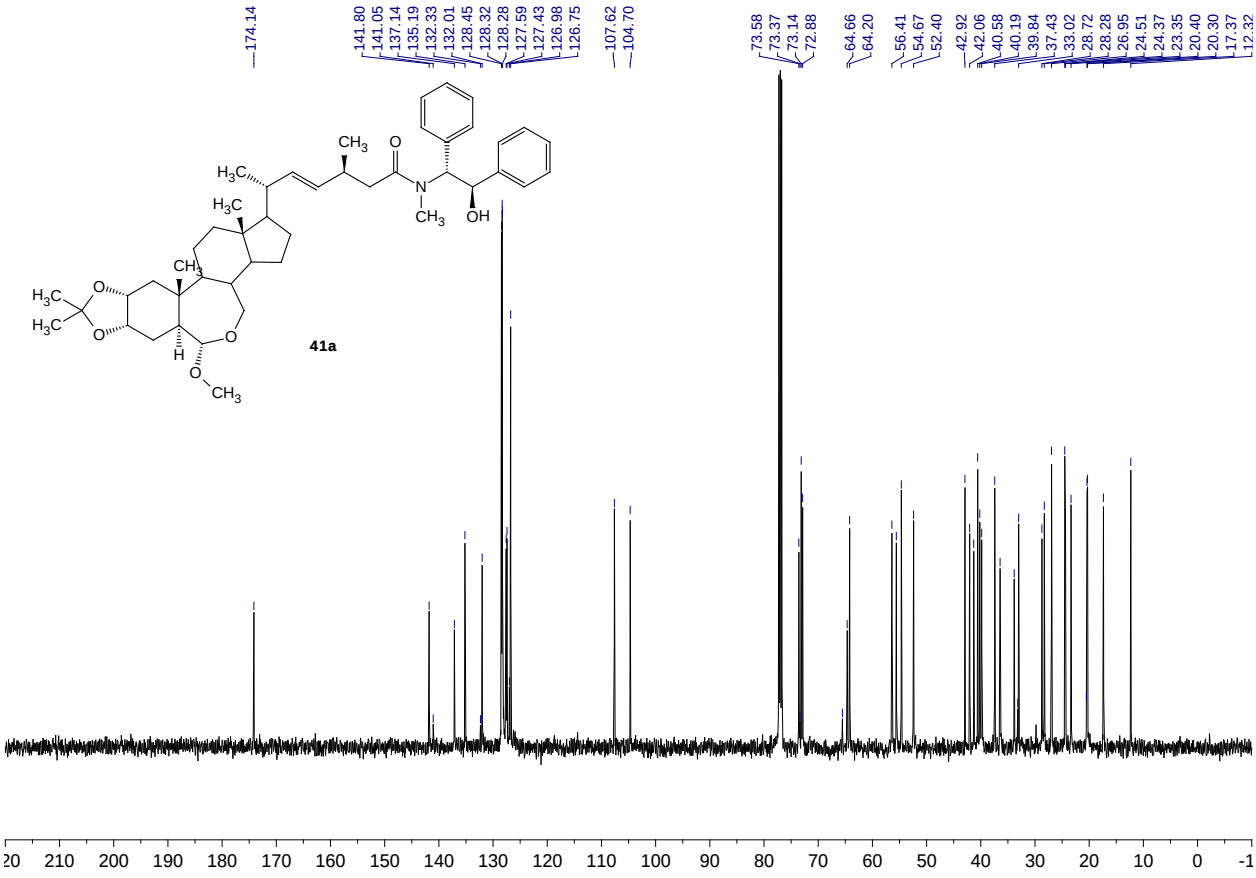
0.75
0.96
1.95
0.11
1.99
1.00
0.72
0.99
1.02
3.05
0.37
2.48
0.91
0.87
1.03
1.09
3.01
2.06
1.09
1.07
3.07
1.91
8.45
3.16
8.98
2.92


41a
174.14
141.80
141.05
137.14
135.19
132.33
132.01
128.45
128.32
128.28
127.59
127.43
126.98
126.75
107.62
104.70
73.58
73.37
73.14
72.88
64.66
64.20
56.41
54.67
52.40
42.92
42.06
40.58
40.19
39.84
37.43
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28.72
28.28
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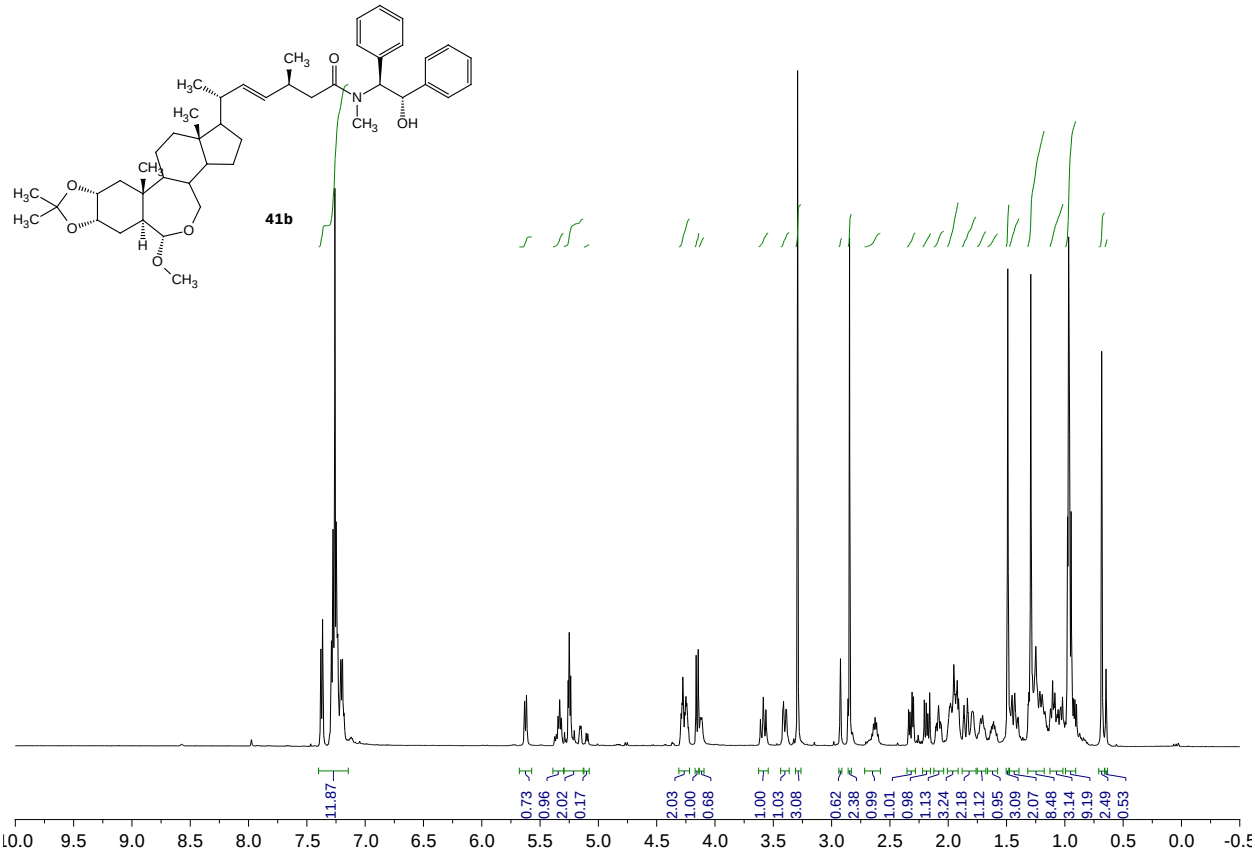
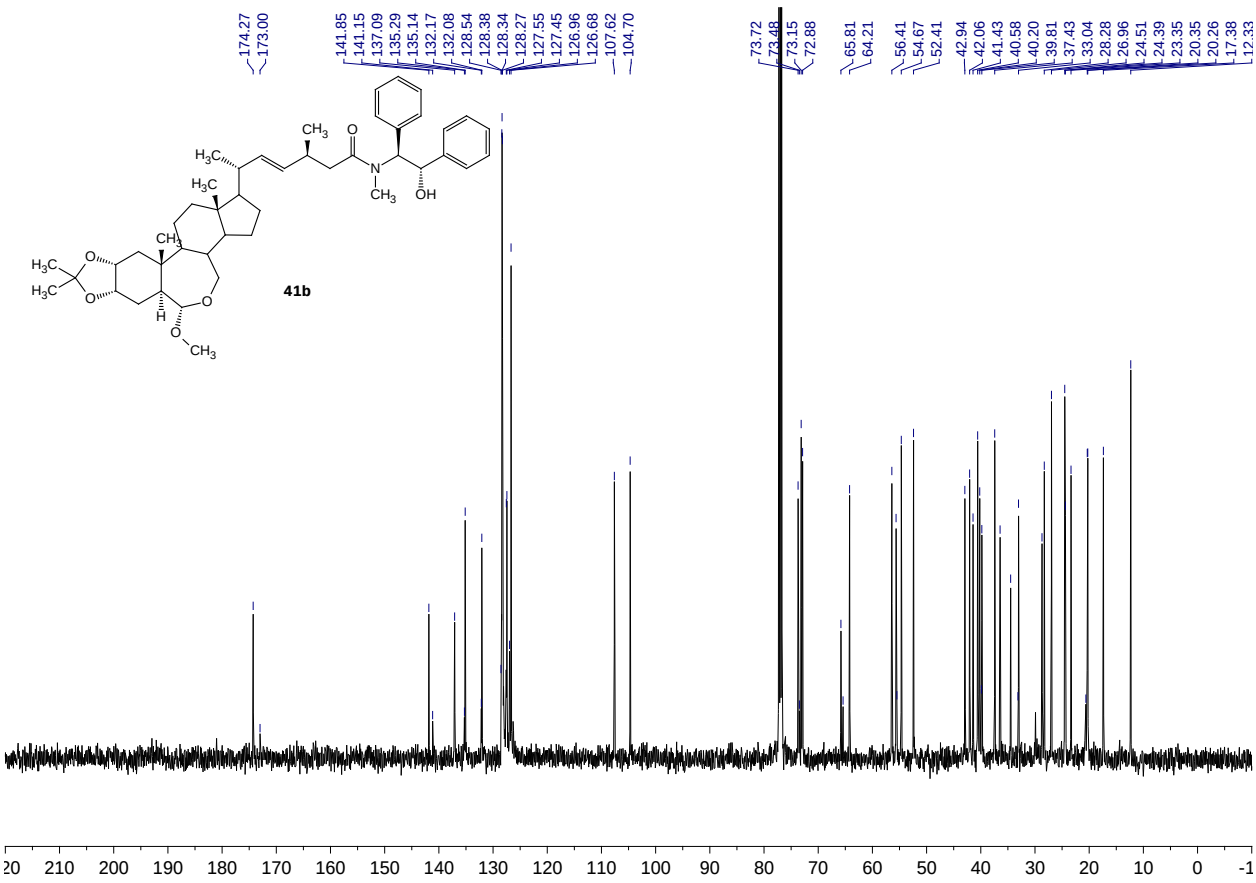
23.35
20.40
20.30
17.37
12.32


41b
11.87
0.73
0.96
2.02
0.17
2.03
1.00
0.68
1.00
1.03
3.08
0.62
2.38
0.99
1.01
0.98
1.13
3.24
2.18
1.12
0.95
3.09
2.07
8.48
3.14
9.19
2.49
0.53


41b
174.27
173.00
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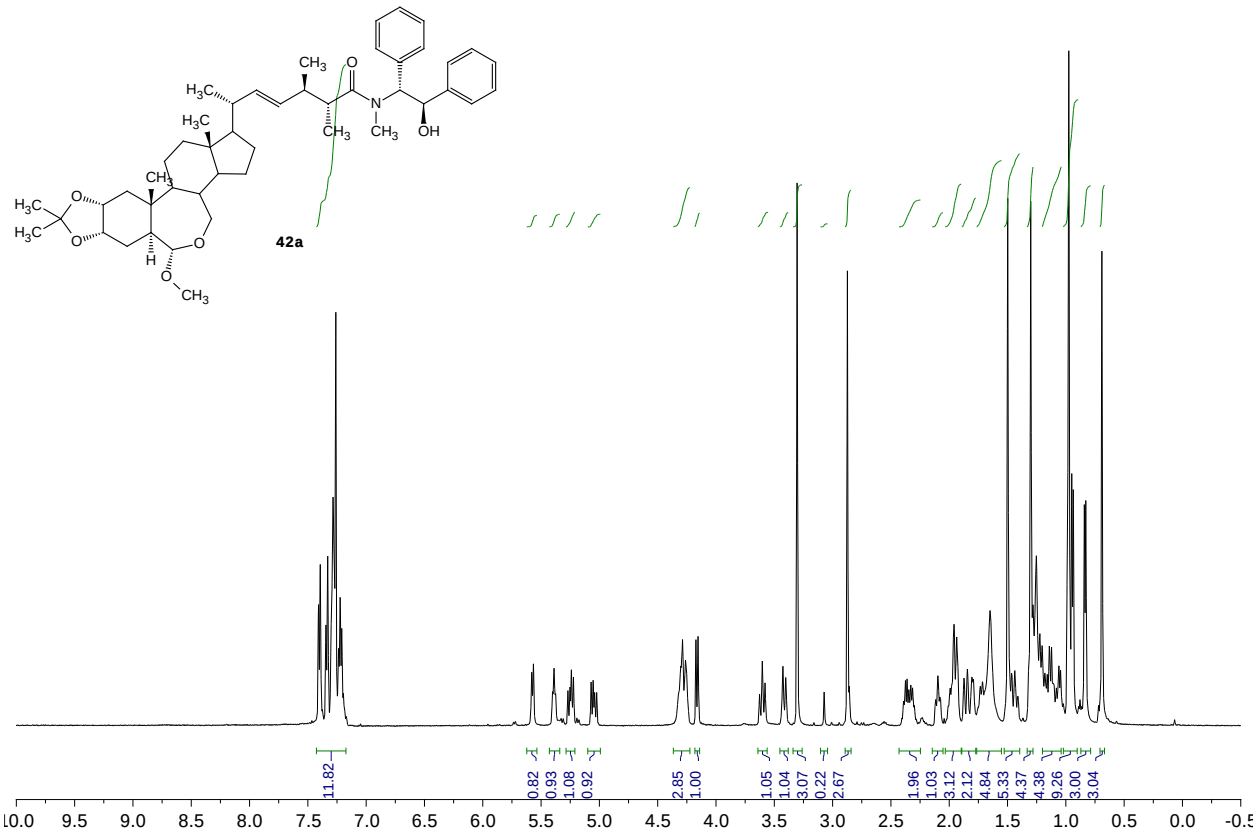
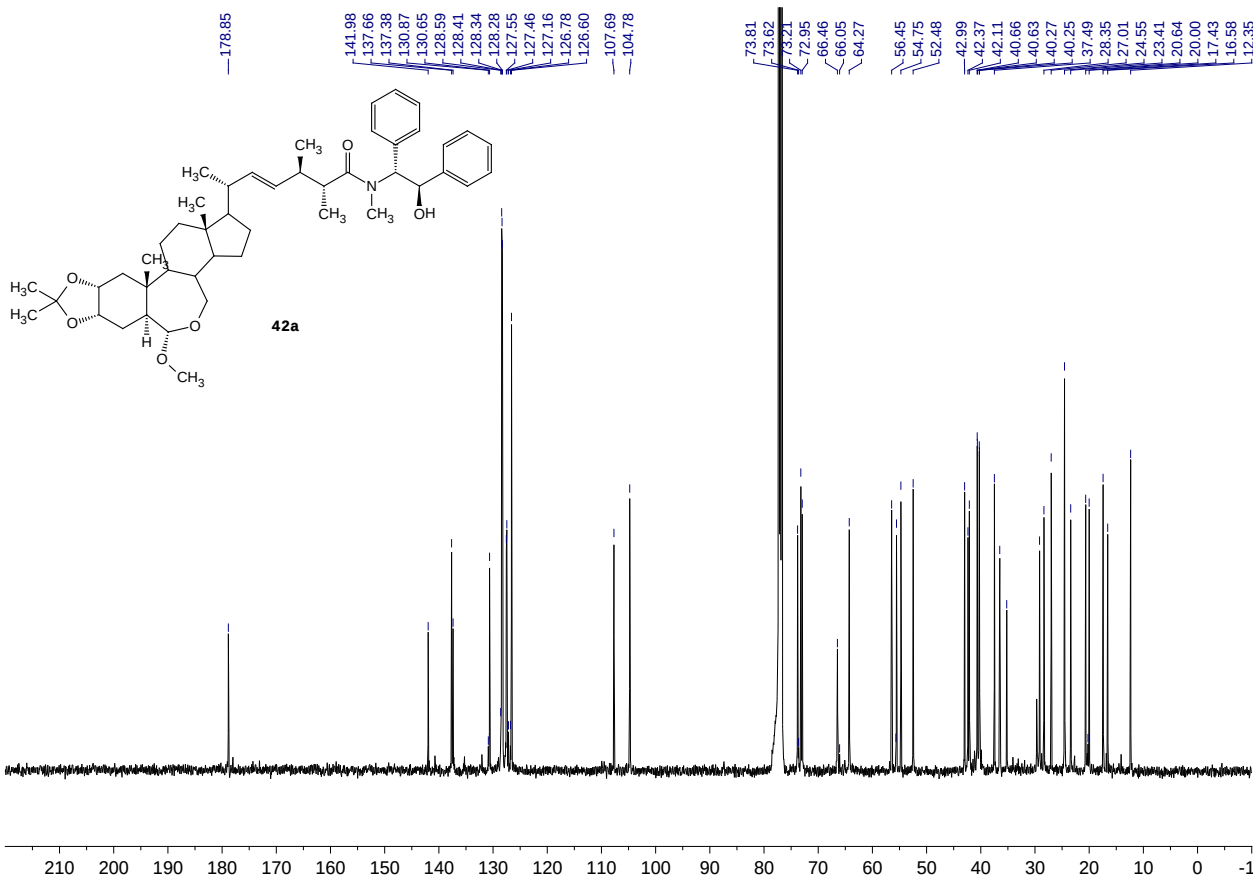
137.09
135.29
135.14
132.17
132.08
128.54
128.38
128.34
128.27
127.55
127.45
126.96
126.68
107.62
104.70
73.72
73.48
73.15
72.88
65.81
64.21
56.41
54.67
52.41
42.94
42.06
41.43
40.58
40.20
39.81
37.43
33.04
28.28
26.96
24.51
24.39
23.35
20.35
20.26
17.38
12.33


42a
11.82
0.82
0.93
1.08
0.92
2.85
1.00
1.05
1.04
3.07
0.22
2.67
1.96
1.03
3.12
2.12
4.84
5.33
4.37
4.38
9.26
3.00
3.04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137.66
137.38
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128.41
128.34
128.28
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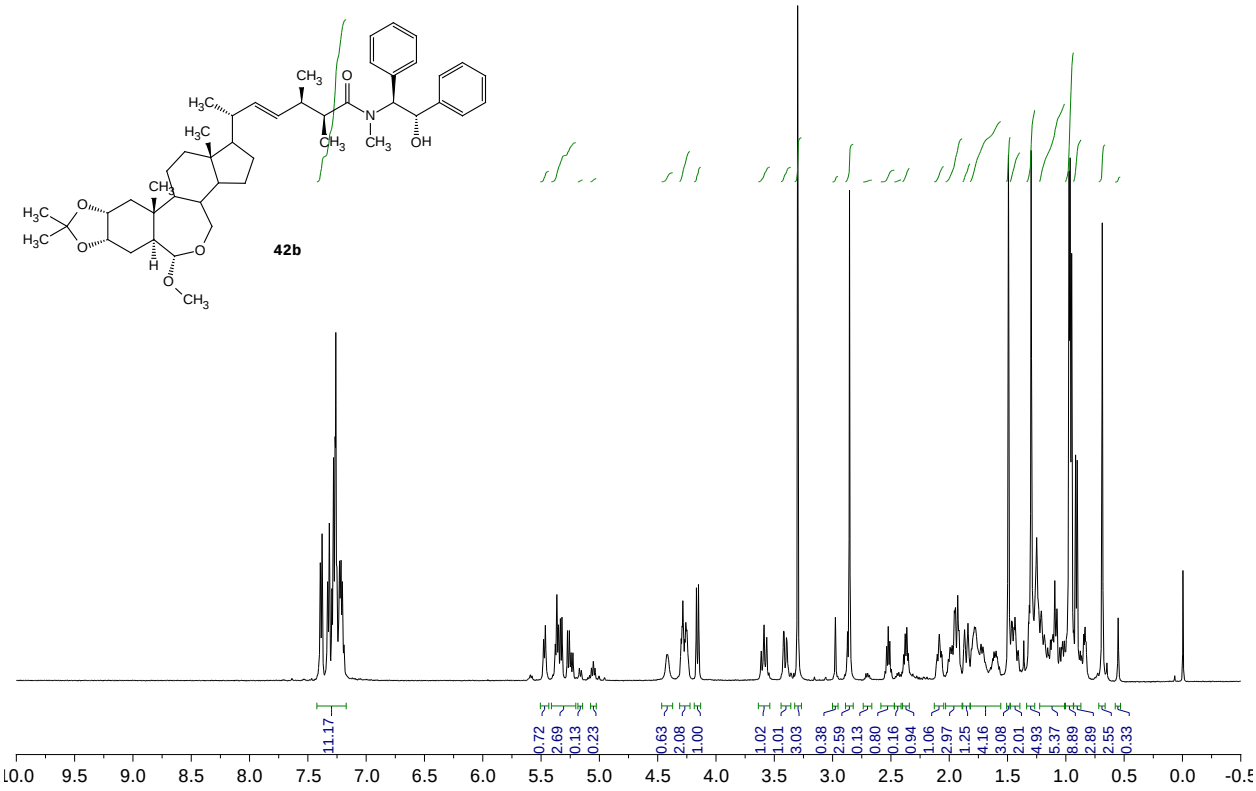
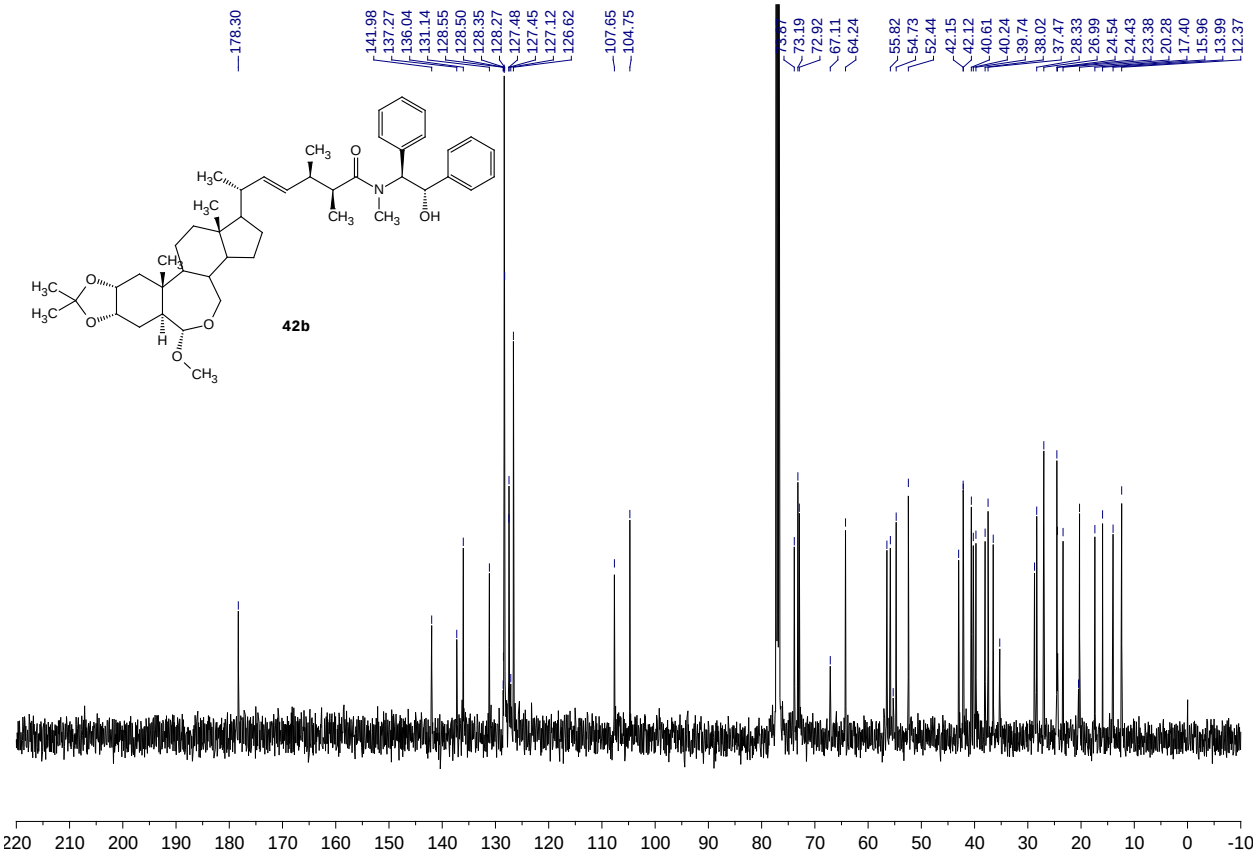
127.46
127.16
126.78
126.60
107.69
104.78
73.81
73.62
73.21
72.95
66.46
66.05
64.27
56.45
54.75
52.48
42.99
42.37
42.11
40.66
40.63
40.27
40.25
37.49
28.35
27.01
24.55
23.41
20.64
20.00
17.43
16.58
12.35
42a


42b
11.17
0.72
2.69
0.13
0.23
0.63
2.08
1.00
1.02
1.01
3.03
0.38
2.59
0.13
0.80
0.16
0.94
1.06
2.97
1.25
4.16
3.08
2.01
4.93
5.37
8.89
2.89
2.55
0.33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137.27
136.04
131.14
128.55
128.50
128.35
128.27
127.48
127.45
127.12
126.62
107.65
104.75
73.87
73.19
72.92
67.11
64.24
55.82
54.73
52.44
42.15
42.12
40.61
40.24
39.74
38.02
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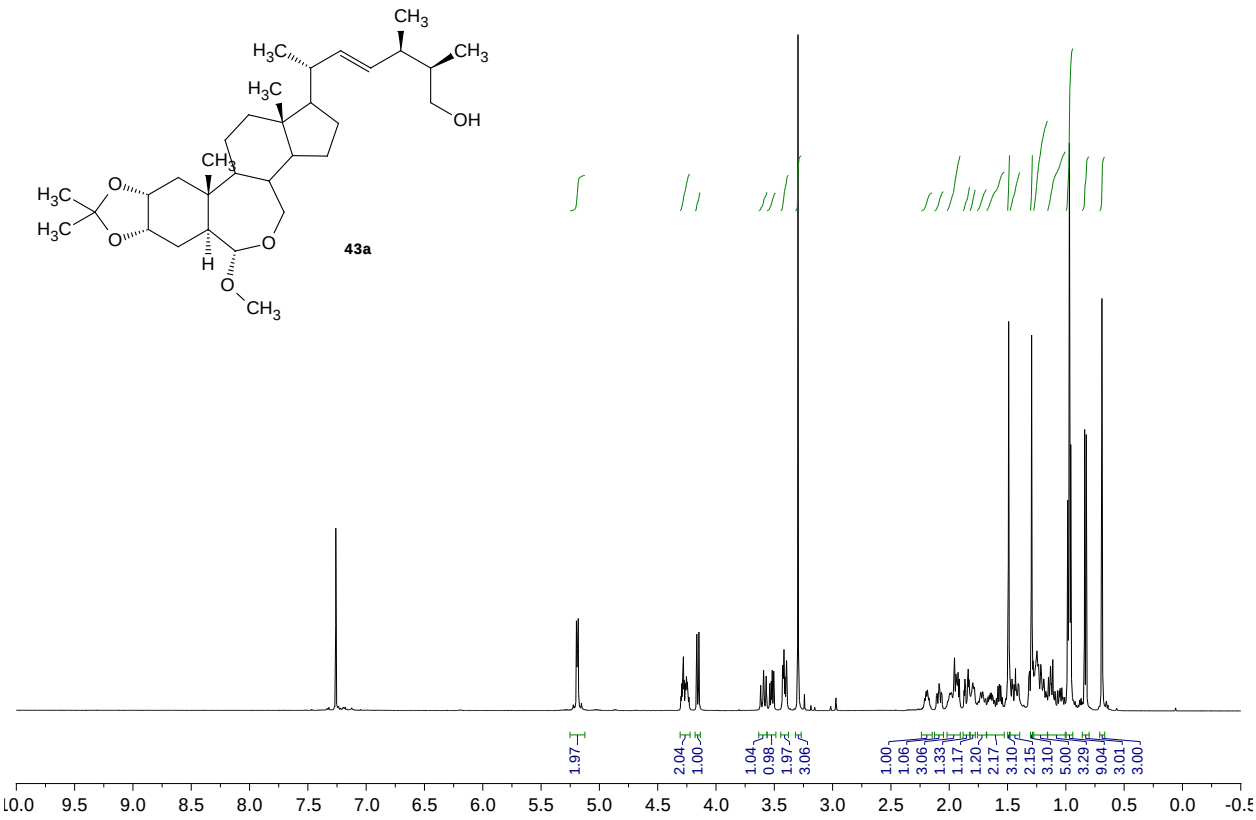
28.33
26.99
24.54
24.43
23.38
20.28
17.40
15.96
13.99
12.37


43a
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2.04
1.00
1.04
0.98
1.97
3.06
1.00
1.06
3.06
1.33
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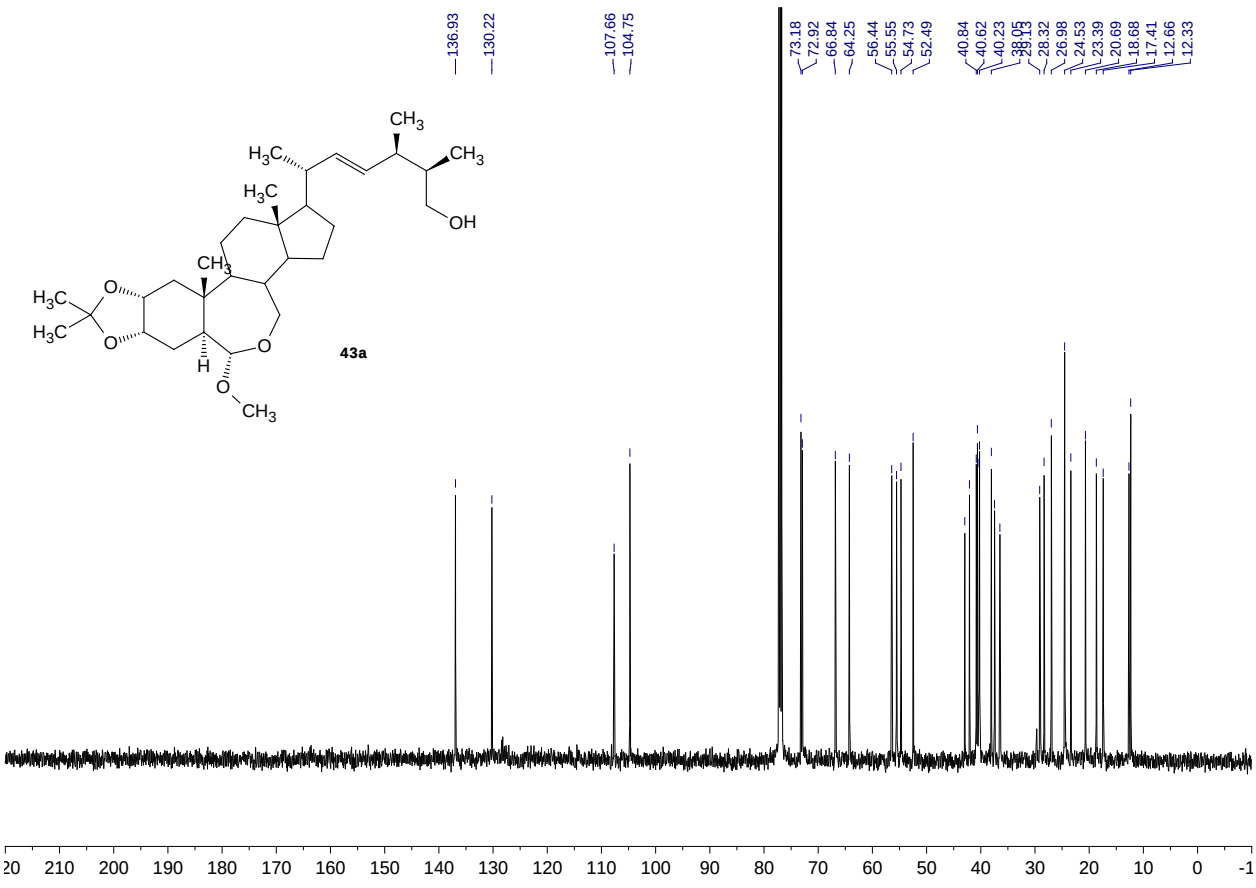
1.20
2.17
3.10
2.15
3.10
5.00
3.29
9.04
3.01
3.00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130.22
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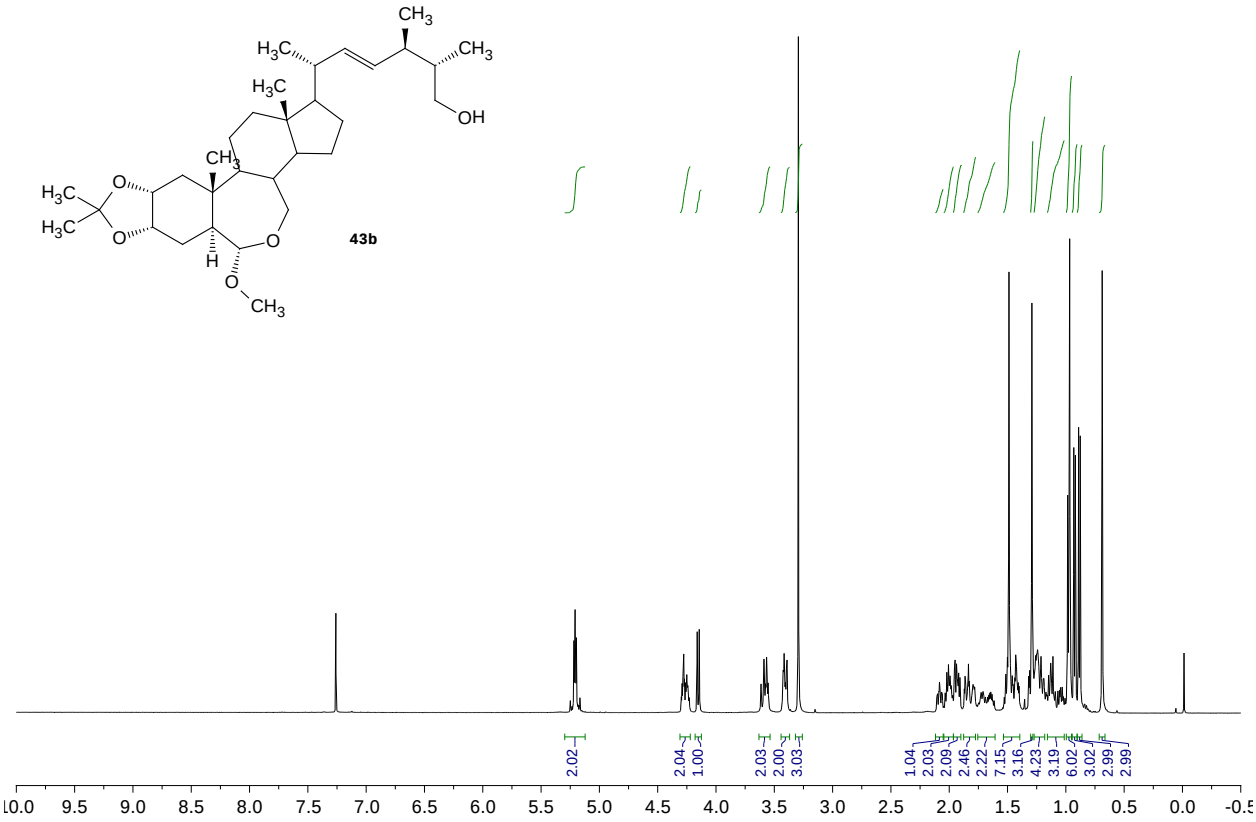
73.18
72.92
66.84
64.25
56.44
55.55
54.73
52.49
40.84
40.62
40.23
38.05
29.13
28.32
26.98
24.53
23.39
20.69
18.68
17.41
12.66
12.33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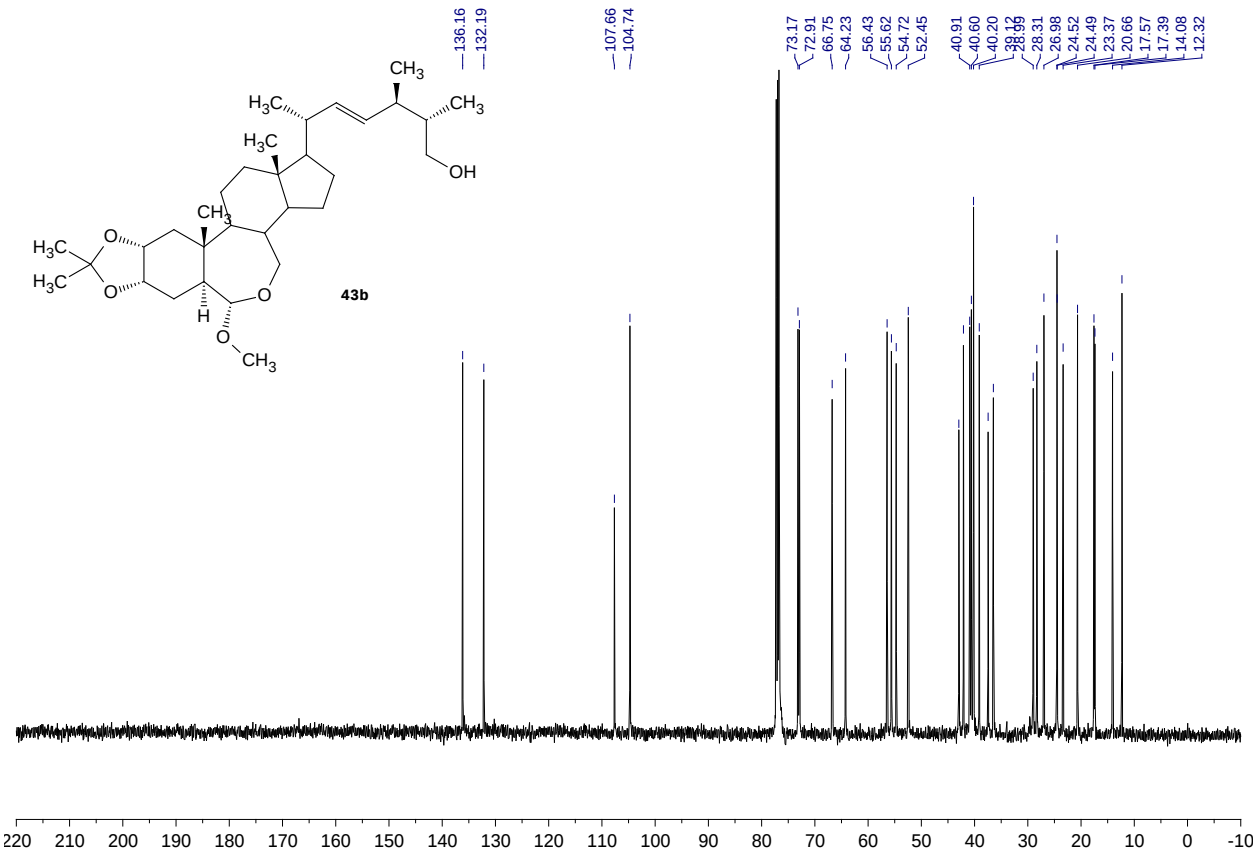
2.04
1.00
2.03
2.00
3.03
1.04
2.03
2.09
2.46
2.22
7.15
3.16
4.23
3.19
6.02
3.02
2.99
2.99


43b
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132.19
107.66
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73.17
72.91
66.75
64.23
56.43
55.62
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52.45
40.91
40.60
40.20
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28.31
26.98
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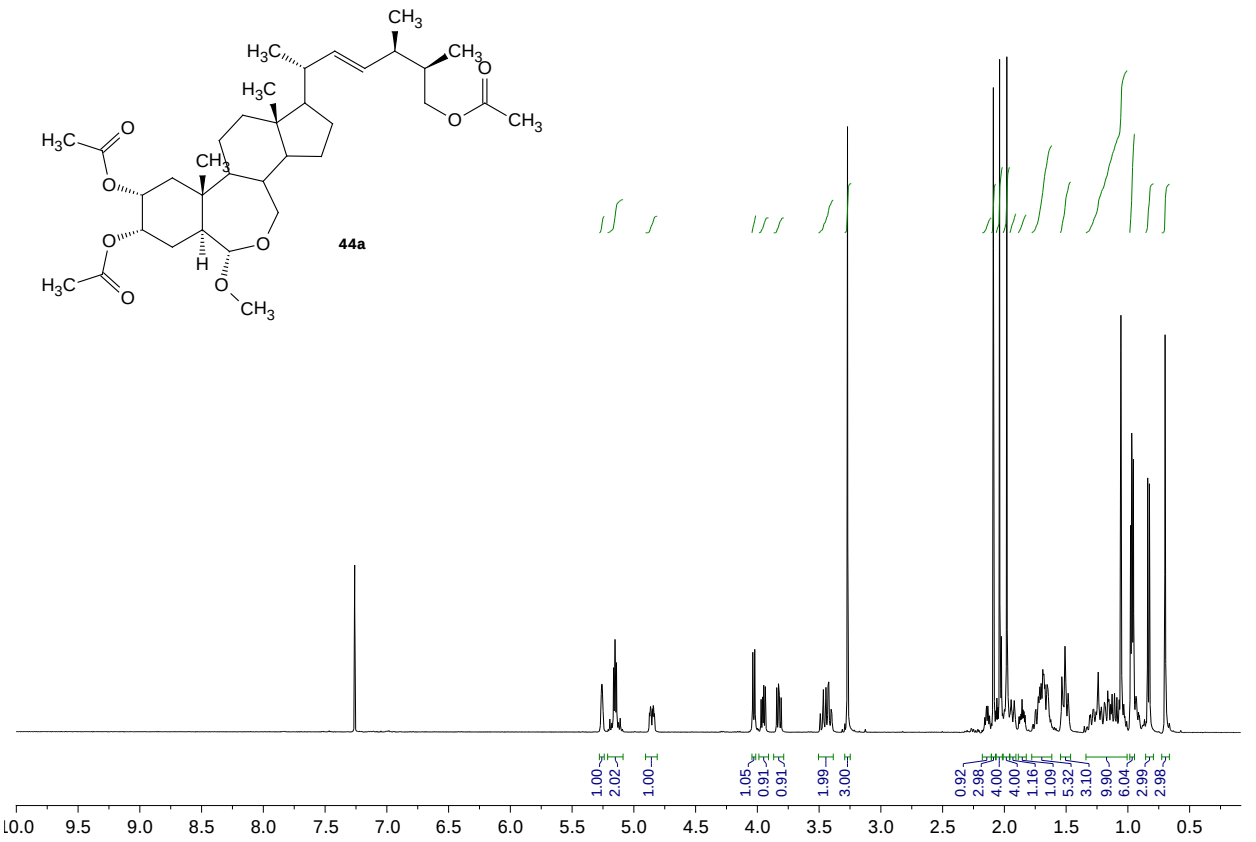
24.49
23.37
20.66
17.57
17.39
14.08
12.32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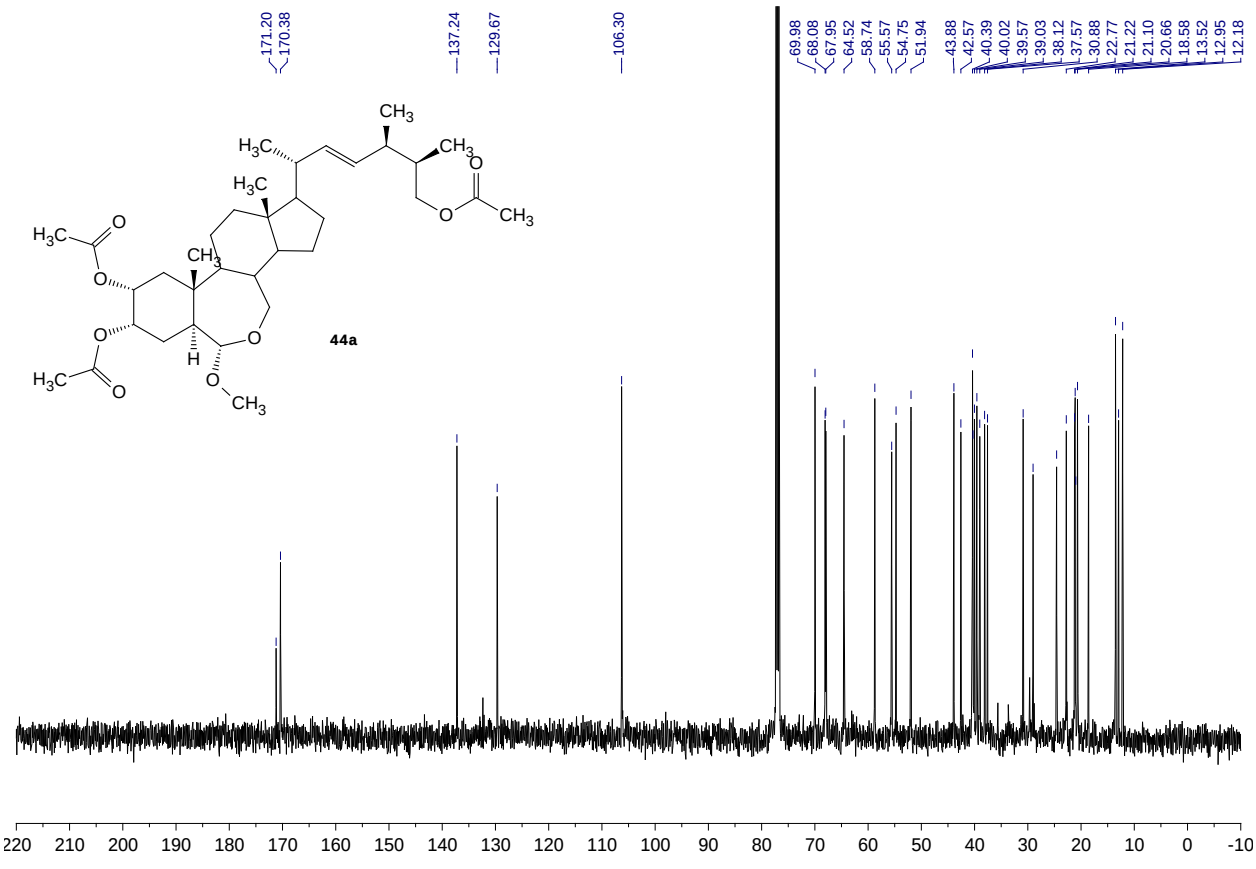
2.02
1.00
1.05
0.91
0.91
1.99
3.00
0.92
2.98
4.00
4.00
1.16
1.09
5.32
3.10
9.90
6.04
2.99
2.98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69.98
68.08
67.95
64.52
58.74
55.57
54.75
51.94
43.88
42.57
40.39
40.02
39.57
39.03
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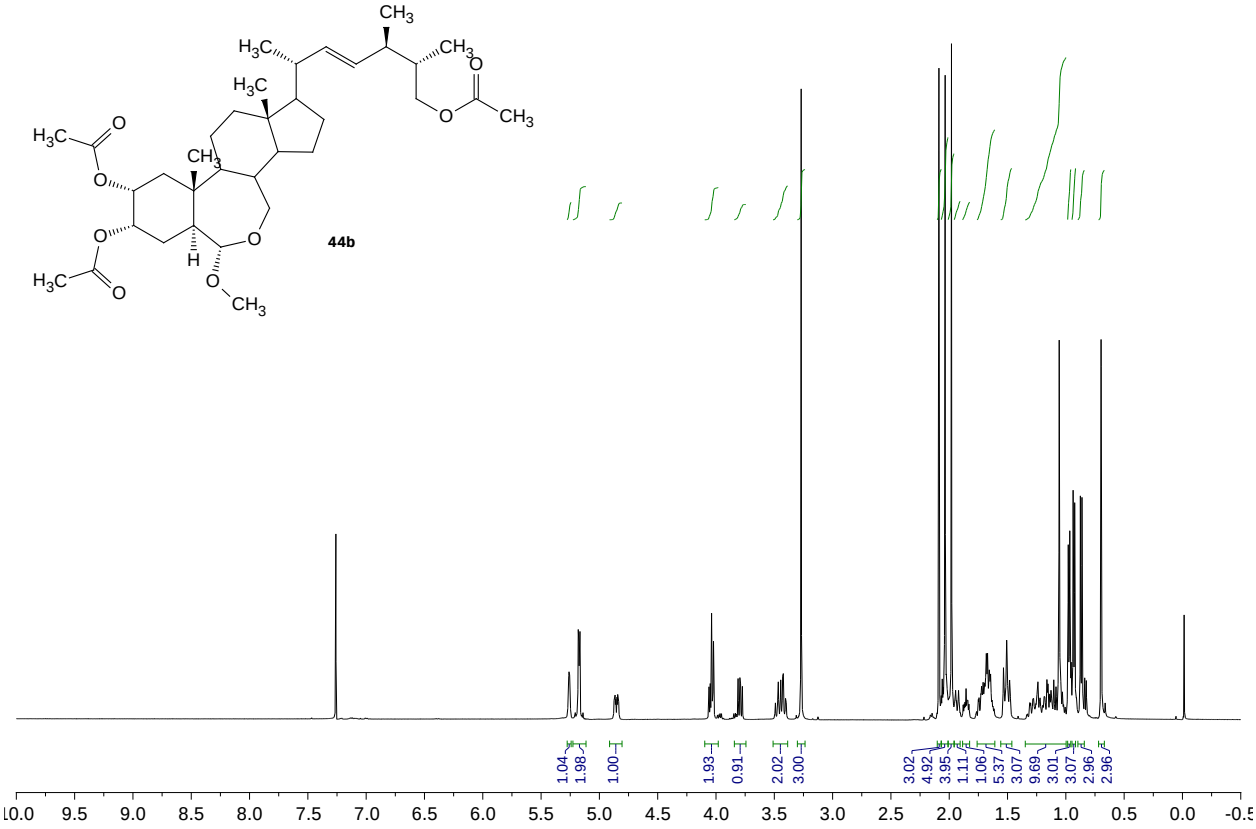
20.66
18.58
13.52
12.95
12.18
44a


44b
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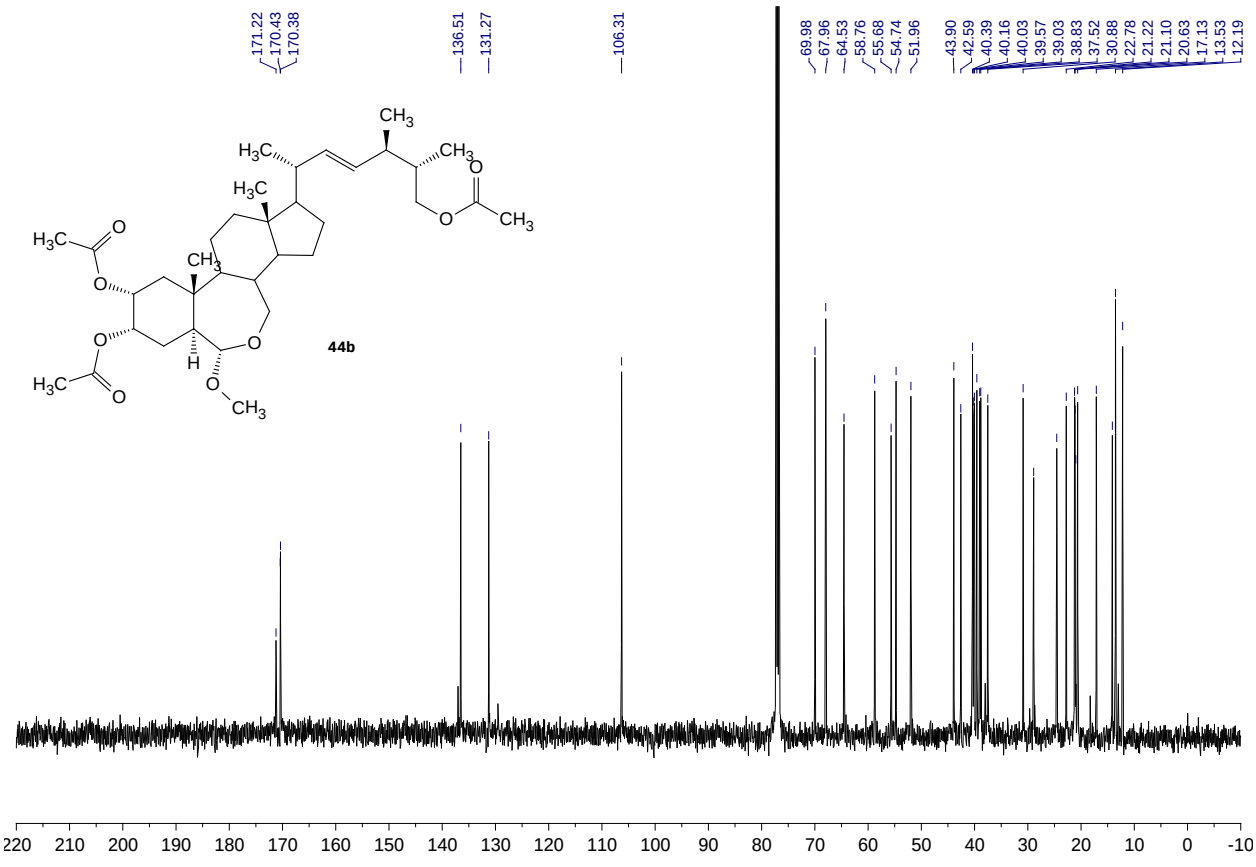
1.98
1.00
1.93
0.91
2.02
3.00
3.02
4.92
3.95
1.11
1.06
5.37
3.07
9.69
3.01
3.07
2.96
2.96


44b
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131.27
106.31
69.98
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64.53
58.76
55.68
54.74
51.96
43.90
42.59
40.39
40.16
40.03
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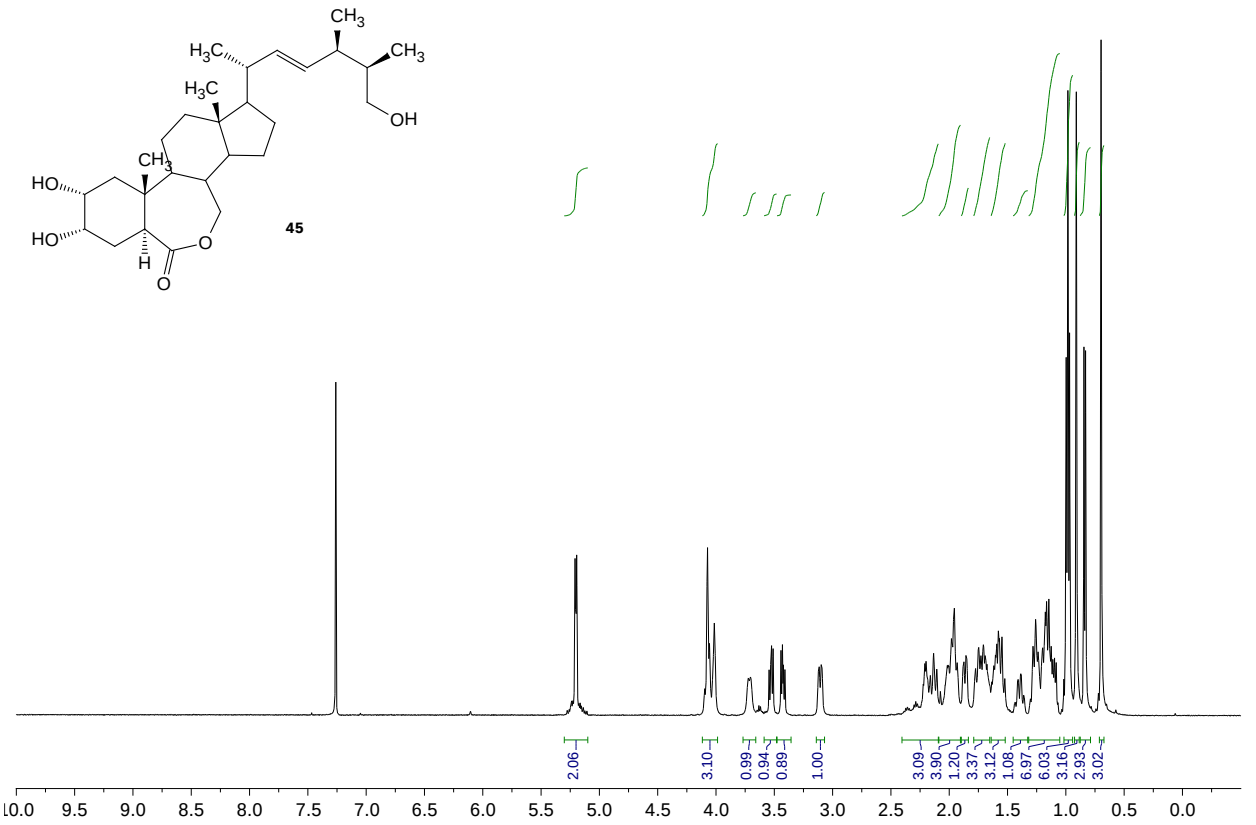
21.22
21.10
20.63
17.13
13.53
12.19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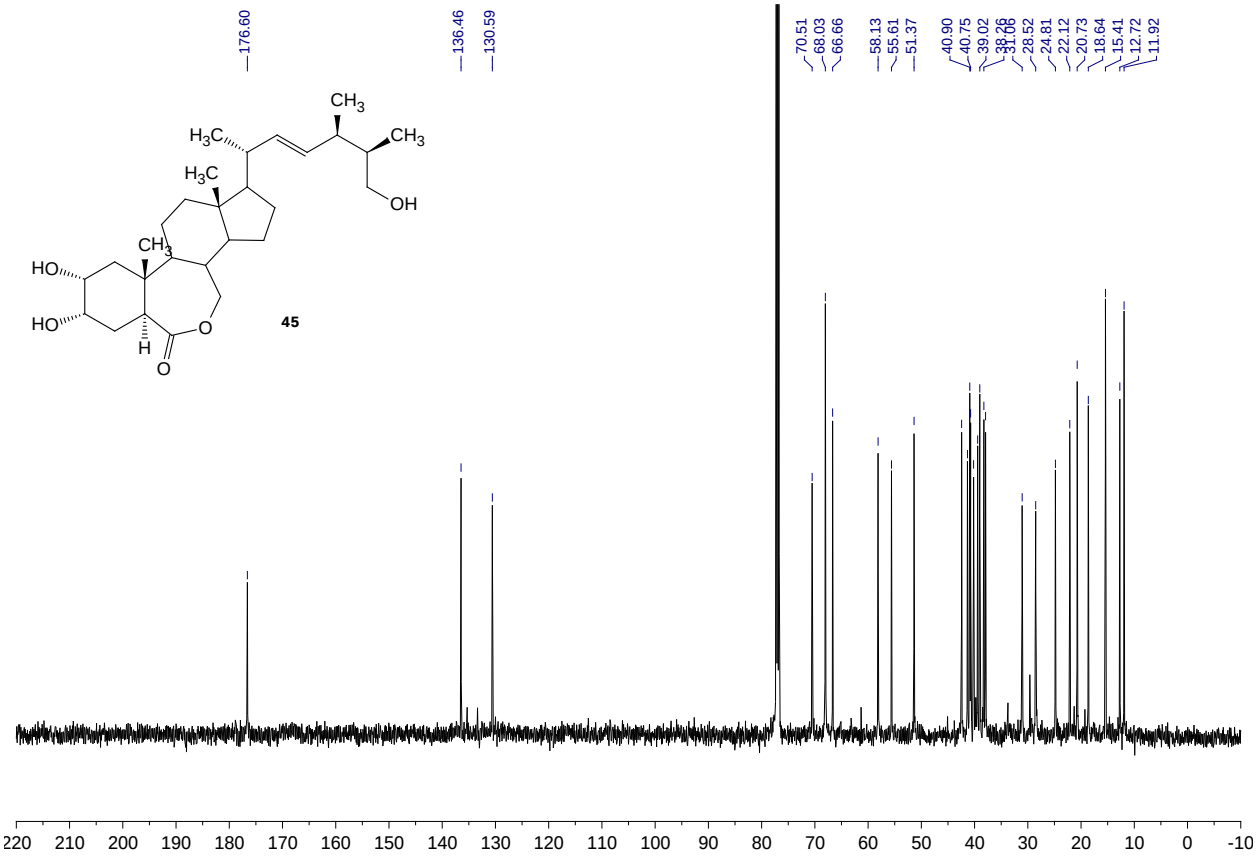
CH3
HO
HO
H
O
O
45
2.06
3.10
0.99
0.94
0.89
1.00
3.09
3.90
1.20
3.37
3.12
1.08
6.97
6.03
3.16
2.93
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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130.59
70.51
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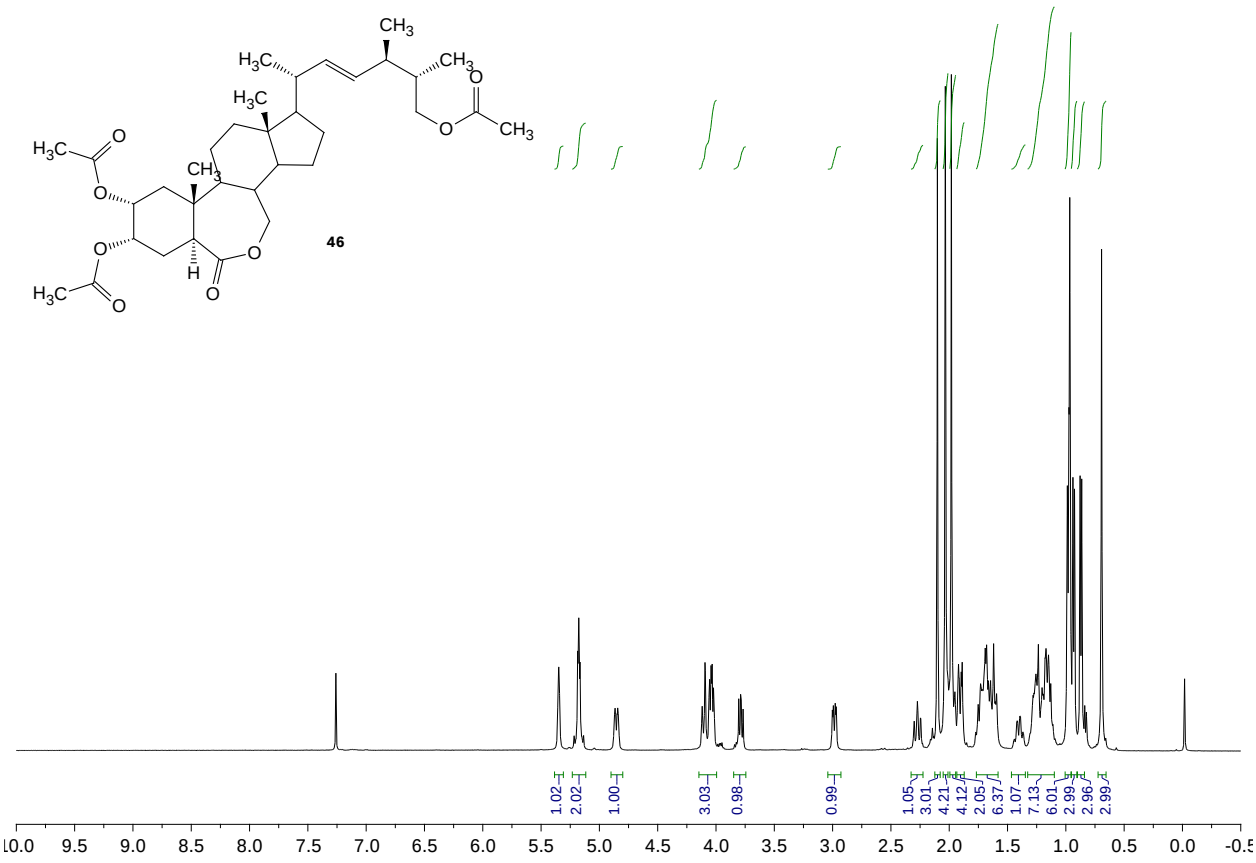
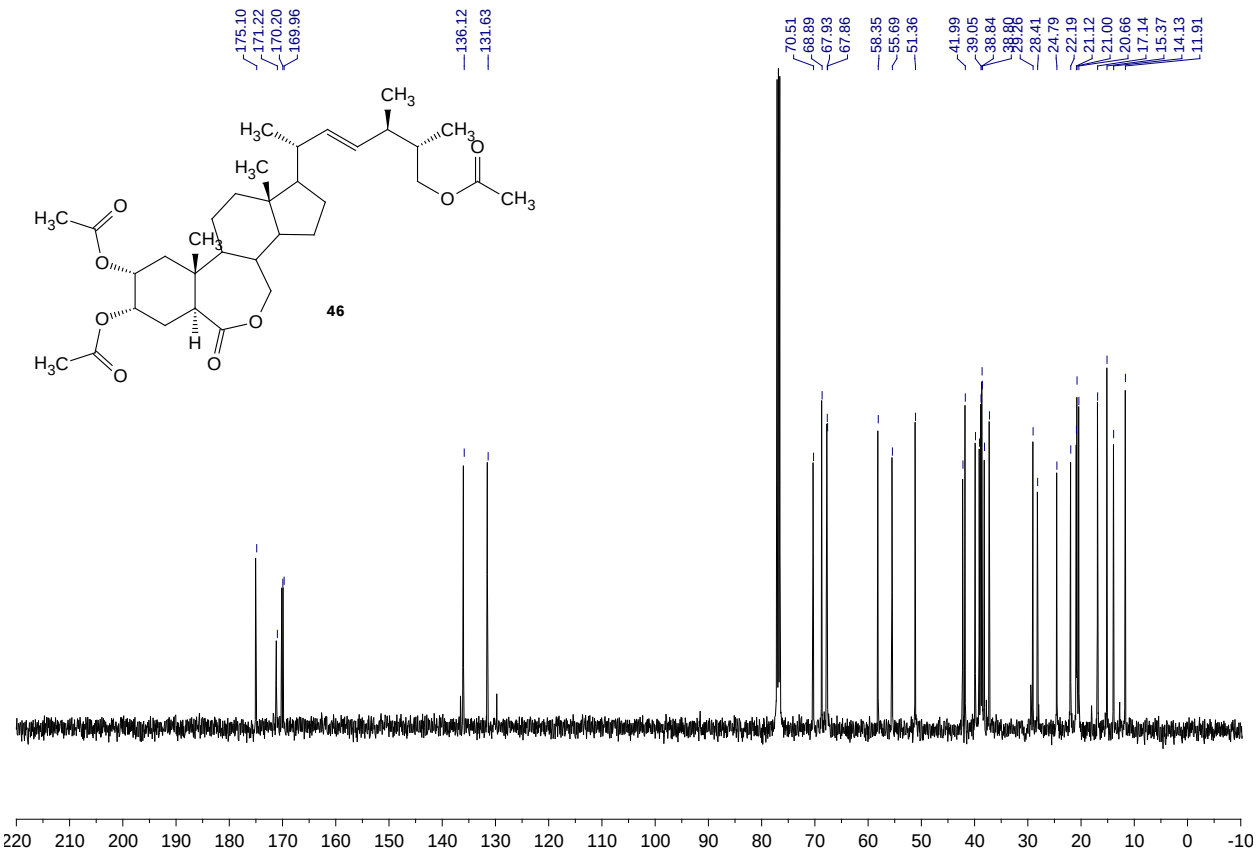
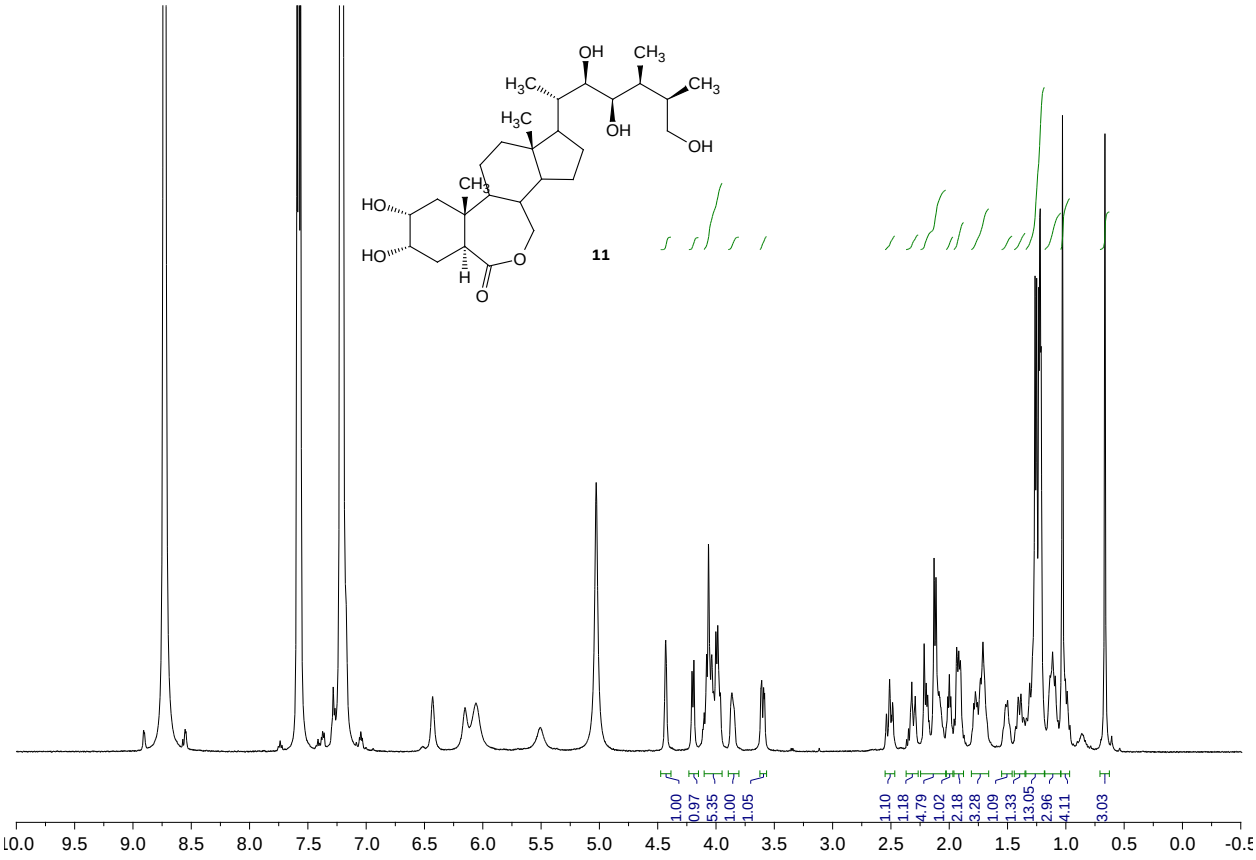
58.13
55.61
51.37
40.90
40.75
39.02
38.26
31.08
28.52
24.81
22.12
20.73
18.64
15.41
12.72
11.92
CH3
H3C
CH3
H3C
OH
CH3
HO
HO
H
O
O
45
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


46
1.02
2.02
1.00
3.03
0.98
0.99
1.05
3.01
4.21
4.12
2.05
6.37
1.07
7.13
6.01
2.99
2.96
2.99


175.10
171.22
170.20
169.96
136.12
131.63
70.51
68.89
67.93
67.86
58.35
55.69
51.36
41.99
39.05
38.84
28.41
24.79
22.19
21.12
21.00
20.66
17.14
15.37
14.13
11.91
46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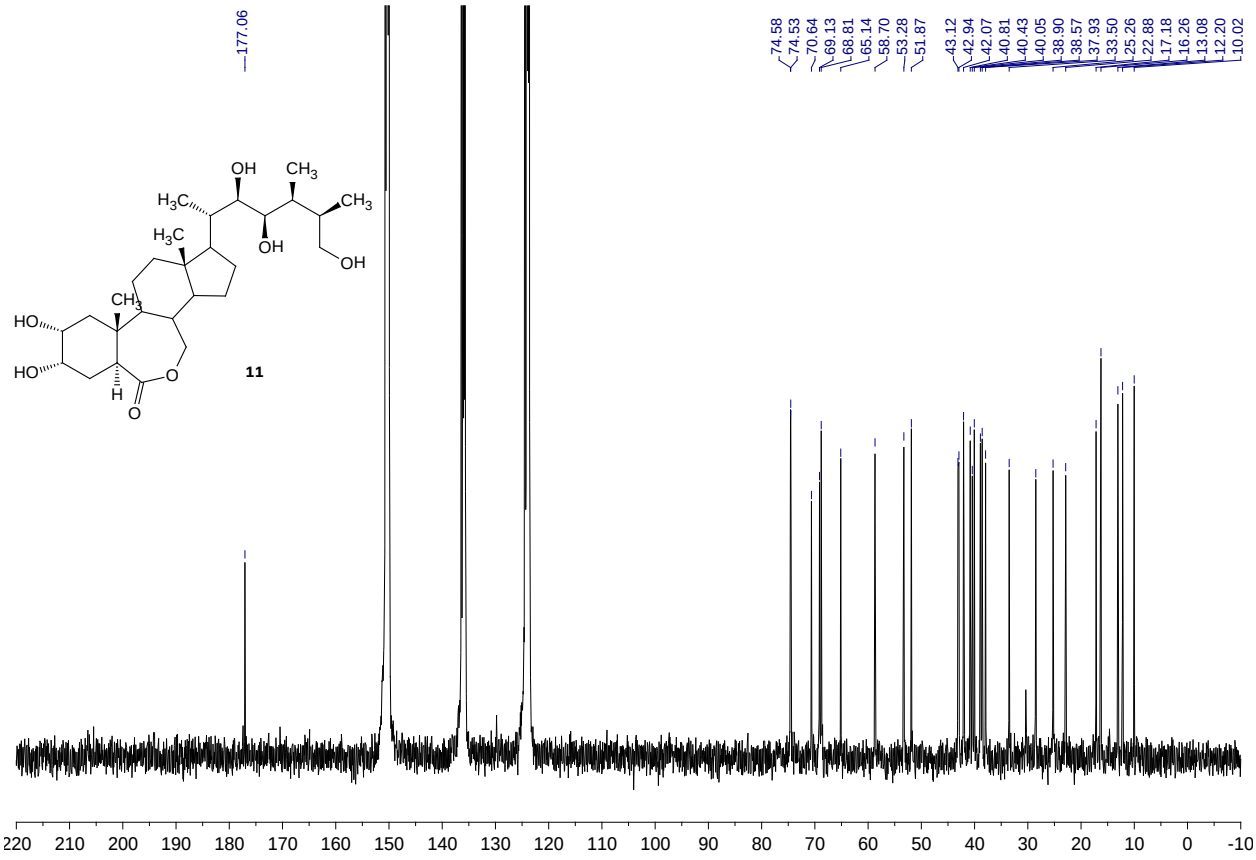
H3C
CH3
H3C
OH
OH
CH3
HO
HO
H
O
O
11
1.00
0.97
5.35
1.00
1.05
1.10
1.18
4.79
1.02
2.18
3.28
1.09
1.33
13.05
2.96
4.11
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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68.81
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51.87
43.12
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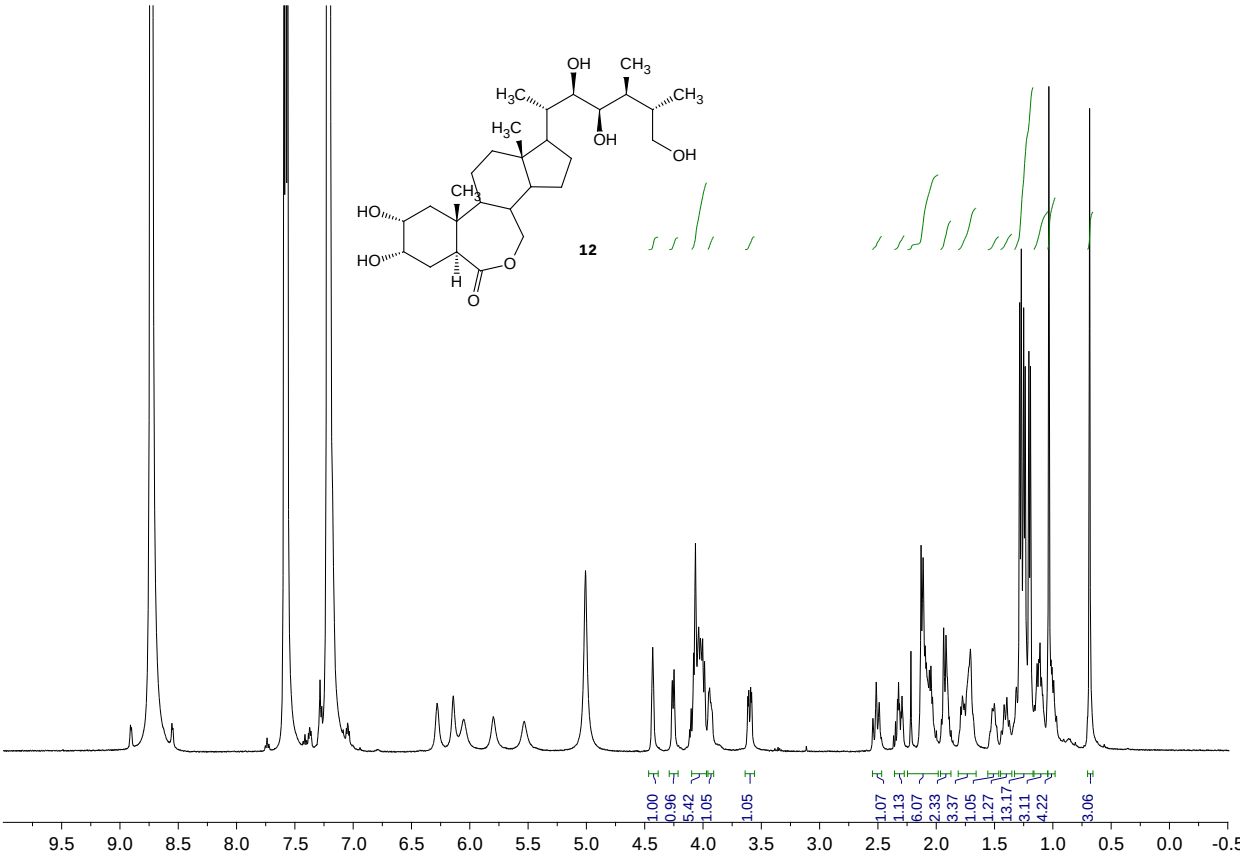
42.07
40.81
40.43
40.05
38.90
38.57
37.93
33.50
25.26
22.88
17.18
16.26
13.08
12.20
10.02
OH
CH3
H3C
CH3
H3C
OH
OH
CH3
HO
HO
H
O
O
11
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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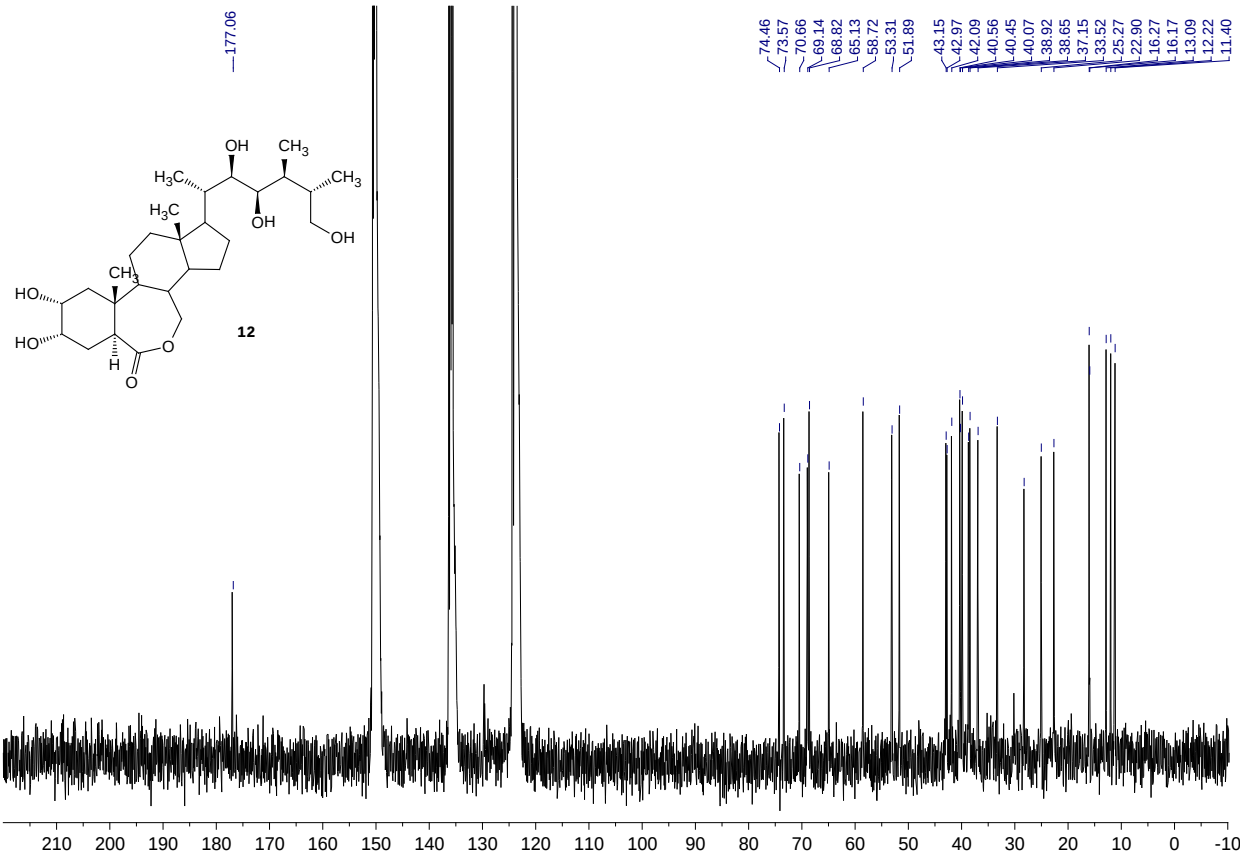
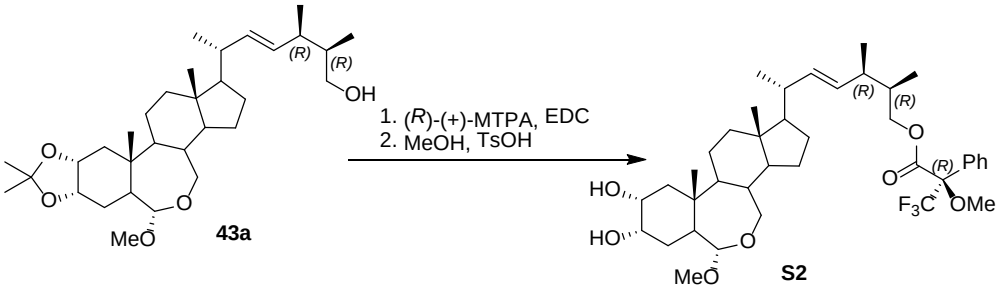
H3C
CH3
H3C
OH
OH
CH3
HO
HO
H
O
O
12
1.00
0.96
5.42
1.05
1.05
1.07
1.13
6.07
2.33
3.37
1.05
1.27
13.17
3.11
4.22
3.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


177.06
74.46
73.57
70.66
69.14
68.82
65.13
58.72
53.31
51.89
43.15
42.97
42.09
40.56
40.45
40.07
38.92
38.65
37.15
33.52
25.27
22.90
16.27
16.17
13.09
12.22
11.40
OH
CH3
H3C
CH3
H3C
OH
OH
CH3
HO
HO
H
O
O
12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

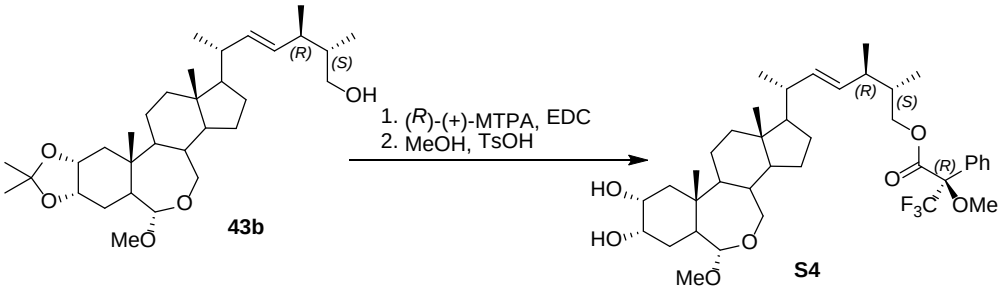
Determination of diastereomeric purity of 43a and 43b

Diastereomeric purity of **43a** and **43b** was determined by ^{1}H NMR analysis of derivatives **S2** and **S4** in $CDCl_3$ based on the peaks of one of the C-26 proton. The corresponding peaks (δ 4.20 for **S2** and δ 4.26 for **S4**) (Fig. S1) were sufficiently resolved to be easily integrated. The amounts of the (25*S*)-diastereomer in **S2** and (25*R*)-diastereomer in **S4** were below the detection limit corresponding to a diastereomeric excess of >99%.



(*E*,25*R*)-2α,3α-Isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene 26-((2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate) (S2). 4-Dimethylaminopyridine (21.4 mg, 0.175 mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (25.2 mg, 0.131 mmol) and (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (20.5 mg, 87.6 μmol) in CH_2Cl_2 (0.5 mL) were added sequentially to a solution of alcohol **43a** (22.7 mg, 43.8 μmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was kept for 12 h at room temperature, then diluted with CH_2Cl_2 (1 mL) and H_2O (1 mL). The organic layer was separated, dried over Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel (PE/EtOAc 5:1 – 2:1) to give **(*E*,25*R*)-2α,3α-dihydroxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene 26-((2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate) (S1)** (17.0 mg, 53%) as colorless oil.

p-Toluenesulfonic acid monohydrate (1.3 mg, 6.94 μmol) was added to the solution of **S1** (17.0 mg, 23.1μmol) in methanol (2 ml). The reaction mixture was kept for 30 min at room temperature, treated with Et_3N (9.7 μL) and evaporated under reduced pressure. The resulting residue was purified by column chromatography on SiO_2 ($CHCl_3$/MeOH 20:1) to afford 15.0 mg (49% for two steps) of **S2** as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.55 (m, 2H), 7.37 – 7.43 (m, 3H), 5.06 – 5.15 (m, 2H), 4.20 (dd, *J* = 10.7, 6.6 Hz, 1H), 4.03 – 4.10 (m, 2H), 3.96 (m, 1H), 3.62 – 3.68 (m, 1H), 3.55 (s, 3H), 3.45 – 3.52 (m, 1H), 3.41 (dd, *J* = 12.4, 2.6 Hz, 1H), 3.29 (s, 3H), 1.88 – 2.14 (m, 7H), 1.56 – 1.82 (m, 7H), 1.32 – 1.54 (m, 4H), 1.04 – 1.18 (m, 4H), 1.00 (s, 3H), 0.96 (m, 6H), 0.83 (d, *J* = 6.9 Hz, 3H), 0.70 (s, 3H).



(*E*,25*R*)-2α,3α-Isopropylidenedioxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene 26-((2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate) (S4). 4-Dimethylaminopyridine (18.8 mg, 0.154 mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (22.1 mg, 0.115 mmol) and (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (18.0 mg, 76.8 μmol) in CH_2Cl_2 (0.5 mL) were added sequentially to a solution of alcohol **43b** (19.9 mg, 38.4 μmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was kept for 12 h at room temperature, then diluted with CH_2Cl_2 (1 mL) and H_2O (1 mL). The organic layer was separated, dried over

Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel (PE/EtOAc 5:1 – 2:1) to give **(*E*,25*S*)-2α,3α-dihydroxy-6α-methoxy-B-homo-7-oxa-5α-campest-22-ene 26-((2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate) (S3)** (15.4 mg, 55%) as colorless oil.

p-Toluenesulfonic acid monohydrate (1.2 mg, 6.3 μmol) was added to the solution of **S3** (14.1 mg, 21 μmol) in methanol (2 ml). The reaction mixture was kept for 30 min at room temperature, treated with Et_3N (9.7 μL) and evaporated under reduced pressure. The resulting residue was purified by column chromatography on SiO_2 ($CHCl_3$/MeOH 20:1) to afford 14.1 mg (53% for two steps) of **S4** as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.55 (m, 2H), 7.36 – 7.43 (m, 3H), 5.06 – 5.17 (m, 2H), 4.26 (dd, *J* = 10.7, 4.7 Hz, 1H), 4.10 (dd, *J* = 10.7, 6.9 Hz, 1H), 4.04 (d, *J* = 7.9 Hz, 1H), 3.93 – 3.98 (m, 1H), 3.62 – 3.68 (m, 1H), 3.54 (s, 3H), 3.46 – 3.52 (m, 1H), 3.41 (dd, *J* = 12.4, 2.7 Hz, 1H), 3.29 (s, 3H), 1.87 – 2.09 (m, 7H), 1.56 – 1.80 (m, 7H), 1.35 – 1.54 (m, 4H), 1.05 – 1.18 (m, 4H), 1.00 (s, 3H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.70 (s, 3H).

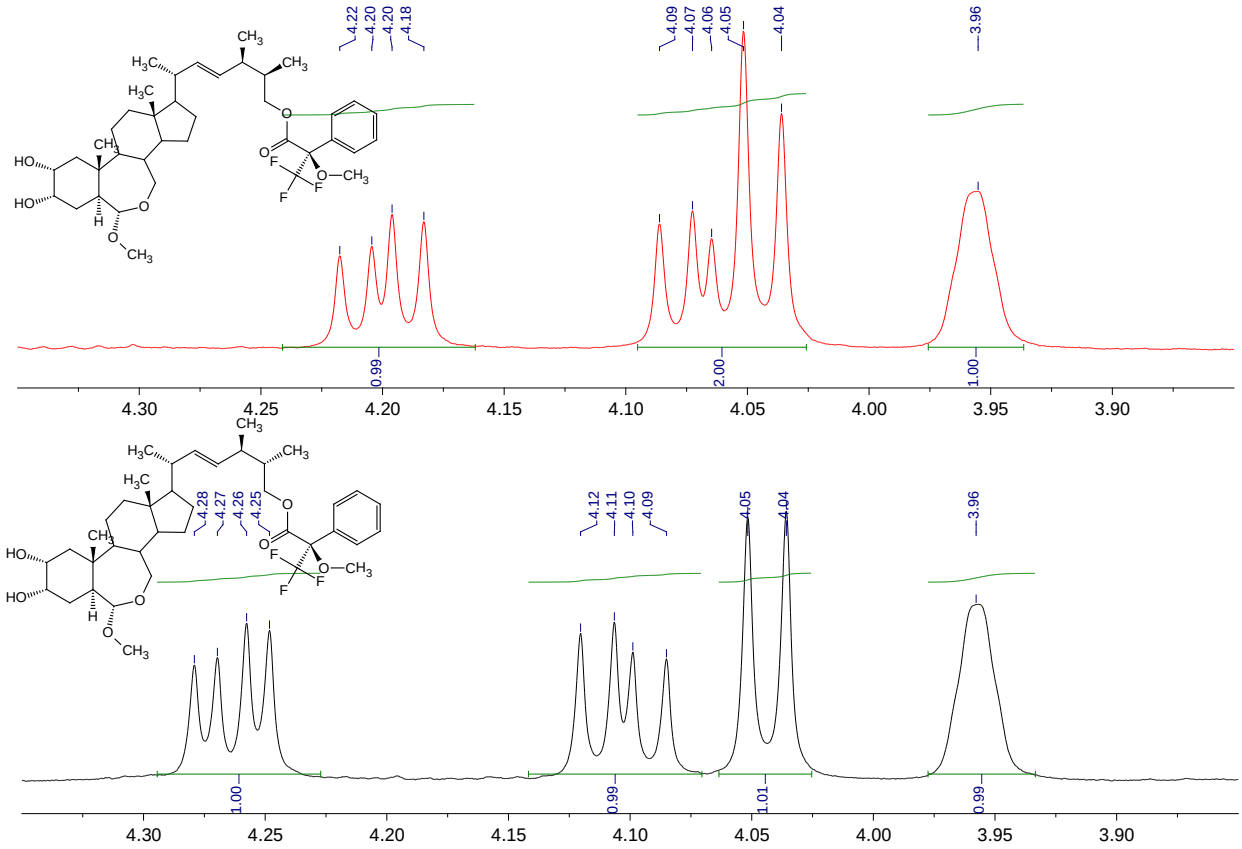


Fig. S1 Fragments of ^{1}H NMR spectra of **43a** and **43b**